secure

Expanding Sustainable Access to Antibiotics

SECURE's Economic and Procurement Tools

February 2024

CONTENTS

EXECUTIVE SUMMARY

SECURE is an innovative initiative being developed by World Health Organization (WHO) and the Global Antibiotic Research and Development Partnership (GARDP) to improve access to both existing and new antibiotics.

SECURE will increase access to a portfolio of quality-assured antibiotics in a sustainable, equitable and appropriate way. It will improve appropriate access to both existing and new antibiotics. SECURE's antibiotic portfolio will be adapted to meet national public health and clinical needs.

Alongside other interventions[1], SECURE is developing economic and procurement tools to incentivize suppliers of antibiotics to enter more country markets. SECURE also aims to provide catalytic financing support to countries for the purchase of antibiotics where affordability is a critical barrier.

To inform the design of SECURE's procurement and economic tools, an analysis was undertaken with the support of the Boston Consulting Group to model the impact and costs of different economic and procurement tools that could be used as part of the overall package of SECURE interventions. A key aim of SECURE is to create market efficiencies and predictability, for example by aggregating antibiotic demand across multiple countries through pooled or coordinated procurement mechanisms. The goal is to optimise pricing and availability for countries by creating a more attractive market for suppliers, while ensuring appropriate stewardship.

This report focuses on the economics of antibiotic product procurement as a building block within SECURE's business model and does not represent a comprehensive description or costing of all other SECURE interventions. For more about our other interventions please refer to the **SECURE 2023 Development Phase update on the SECURE website.**

The model estimated the impact of different packages of economic and procurement tools on both access to, and costs of different antibiotic products. The analysis used several different antibiotic 'archetypes'[2] and evaluated the purchasing costs to participating countries as well as costs incurred by SECURE to set up and operate the mechanism. The model also considered the feasibility of implementing different packages of tools by pressure testing the models with key stakeholders including procurement entities and suppliers. The initial analysis was focused on low- and middle-income countries (LMICs), with the assumption that high-income countries (HICs) may be modelled and included later.

1 See annexure A.

2 Antibiotic Archetypes - Antibiotics that share common features in terms of categorisation as per WHO AWaRe index and similar access challenges or market dynamics.

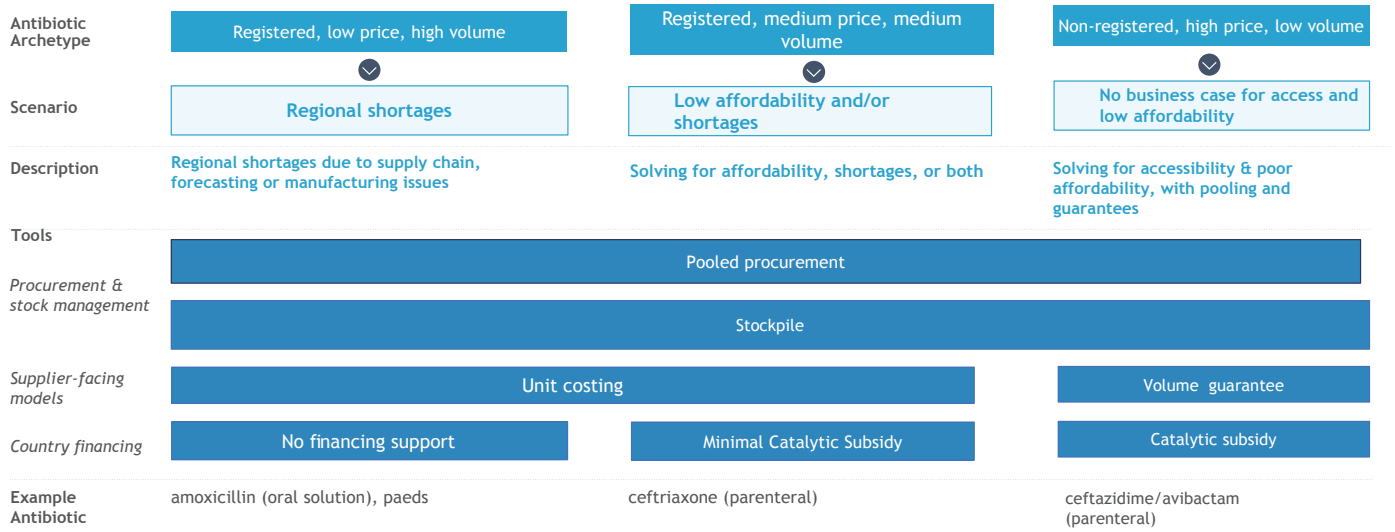
Economic and procurement tools to solve access barriers

From a market perspective, antibiotics are a diverse class of products, ranging from high-volume, low-cost products with many suppliers, to newer products which are low-volume and high-cost and often have a sole supplier. To assist in developing SECURE's economic and procurement tools, three 'antibiotic archetypes' were identified along with their associated key access challenges that could be addressed by SECURE.

- **Archetype 1:** High volume, off-patent antibiotics characterized by low margins. These antibiotics were often in the "Access" category. Recurrent shortages, stemming from inaccurate forecasting, manufacturing constraints, or by suppliers ceasing production, were identified as the most significant barriers.
- **Archetype 2:** Antibiotics that are of medium volume, possibly off-patent. These antibiotics were often classified under the "Watch" category. Challenges to access include factors such as cost considerations relative to national budgets, omission from procurement policies, and frequent product shortages.
- **Archetype 3:** On-patent, typically recently introduced antibiotics, that are used at low volume and are highly priced. These antibiotics are typically "Reserve" or lower volume "Watch" antibiotics. Key challenges hindering access to these products involve prices, financial constraints and inconsistent and segmented demand, leading to limited registration across essential geographical areas.

For each antibiotic archetype, individual economic and procurement tools were identified as potential solutions. Various combinations of economic and procurement tools were tested (see Figure 1 below) and those which could help to address key access barriers most feasibly were chosen.

Figure 1 *Antibiotic Archetypes aligned with economic and procurement tool which were most feasible*



The analysis estimated the impact of different tools for a small LMIC country, with a total population of 12 million, of which 75% (9.3 million) rely on public sector health services. This country was added into a pooled procurement mechanism with an assumed pool of 100 million public sector population. Tunisia was selected as the small country for modelling purposes due to availability of data for the required variables. One sample antibiotic was chosen to represent each archetype in order to use real pricing data to model. Public sector tender prices as well as estimates for consumption volumes for sample antibiotics were available from a representative country to assist in the modelling. This is why the 100 million pool was modelled on the public sector population only.

This model assumes SECURE would partner with an existing procurement entity or entities (including existing regional pooled procurement entities). These would provide services to support country forecasting, pooling of orders, and contracting with suppliers on price and terms. It would also involve ordering and payments; supply and logistics with warehouses containing the stockpiles and transportation to the ports of entry of countries. Thereafter the model assumes that the country would take control of the last mile processes of distribution.

Testing and comparing outputs across different scenarios was only possible by standardising and adding conditions for each model to work. These conditions are critical to achieve the desired impact when implemented. Some of these conditions include:

- The willingness of countries and manufacturers to adopt pooled procurement using an existing procurement entity contracted by SECURE.
- Establishing mechanisms to implement stewardship, availability of diagnostics for laboratory sensitivity testing and monitoring systems for pharmacovigilance.
- Mechanisms to accelerate or harmonize drug registration processes of selected prioritized products across a range of countries including the development of standardized packaging/labelling.
- The existence of a functional in-country distribution and cold chain (where needed) to ensure the drugs reach the patients.

Scenarios showing good potential for SECURE to flexibly address country-specific needs

Provisional findings indicate that SECURE has high potential to support access to antibiotics by implementing the following tools in various combinations to respond to the access barriers per antibiotic archetype: pooled procurement, supplier guarantees, catalytic product subsidies, and stockpiles. The benefits of the SECURE package of interventions, tailored per antibiotic archetype are predicted to include improved affordability for countries, incentivized market entry and predictability of demand for suppliers, surety of supply and quality-assured products available in countries.

The most economically attractive stockpiles in the analysis were revolving stockpiles linked to pooled procurement mechanisms. The supplier guarantee would be based on either a minimum revenue or volume that is sufficiently attractive to register and supply the product in the countries. In the case of the volume guarantee, volumes would be based on forecasts of demand based on appropriate use. Should the minimum revenue needed for suppliers exceed estimated demand, i.e. more volume would need to be guaranteed than what would be required for appropriate use, a revenue guarantee would be more appropriate. In either case of a volume or revenue guarantee, should the demand exceed the minimum volumes determined in either the volume or revenue guarantee, then the product will be paid for at a unit cost at the agreed price. This is similar to the Sweden model of revenue guarantee.

Ultimately, a balanced portfolio of “Access”, “Watch” and “Reserve” antibiotics to enhance stewardship and match national treatment guidelines would need to be created. See a brief summary of the most viable scenarios in Figure 2 overleaf. Results are shown in terms of the overall cost savings to those participating in pooling, potential product price reduction, and estimated cost of implementing the mechanism for a period of 5 years.

Figure 2 *Scenarios showing good potential for SECURE to flexibly address country-specific needs*

Antibiotic Archetype	Tools	Antibiotic example (single drug per archetype)	Pooled Country savings over 5 yrs[1]	% price reduction potential[2]	Costs of mechanism over 5 yrs[3]
1. Registered, low price, high volume	Pooled procurement + revolving Stockpile	"Access" antibiotic (amoxycillin oral solution)	USD 4.15 million	16%	USD 3.2 million
2. Registered, medium price, medium volume	Pooled procurement + revolving stockpile + with catalytic subsidy	"Watch" parenteral antibiotic (ceftriaxone IV) (subsidy applied at 25% and declining thereafter)	USD 7.68 million	37%	USD 5.78 million
3. Non-registered, high price, low volume	Pooled procurement + revolving stockpile + supplier guarantee + catalytic subsidy	"Reserve" antibiotic (ceftazidime/avibactam IV) (subsidy applied at 95% and declining thereafter)	USD 8.86 million	>80%	USD 3.64 million + USD *0.748* million[4]

1. Savings calculated at average LMIC price for a small country (e.g.,Tunisia) for an individual antibiotic and summed up for the entire 100 million population pool
2. Discount based on average LMIC price for antibiotic
3. Mechanism includes contracting with an existing Procurement Entity - service fees, stockpile, warehousing and wastage costs
4. SECURE volume guarantee liability should one be included for the countries in the pool

Please note: These numbers are indicative only with large uncertainty margins and are meant to illustrate the potential benefits and costs of different tools.

Tools found to be less feasible

Some economic and procurement tools tested were found to be less feasible. This included using a rotating stockpile for emergency supply without pooling to address global shortages of high-volume Access antibiotics. The costs to run such a stockpile were estimated at USD 15.3 million for 5 years for a single product (modelled on a single strength of amoxicillin capsules) for the pool of 100 million population. This is not likely to be economically feasible or effective, as the choice of stockpile size will depend on the severity of expected shortages and the ability to predict which antibiotics and which countries may be prone to shortages, so that the stockpile can be placed in the correct region.

Risk for mitigation

The models contain risks including:

- Risks relating to the set-up of the procurement entity and mechanism. Countries may be uncertain about the potential benefits, resulting in lack of national political will to participate. To ensure sustainability, country subsidies will need to be continued over a longer period. Suppliers might not be incentivized to agree on price reductions, despite the benefits of market consolidation, improved predictability and supplier guarantees. If there is not sufficient take up by countries or it takes too long to set up, then the economies of scale impacting on pricing may be undermined. To mitigate this risk, SECURE will work with procurement agencies to form long-term relationships with suppliers and implement further interventions that may incentivize supplier engagement.

- Operating risks include inaccurate forecasts and delayed payments or payment defaults by countries. Countries might not adhere to forecasting and stewardship monitoring mechanisms, undermining the ability to preserve the effectiveness of these antibiotics SECURE will need to develop forecasting tools which support country estimates of needs based on a prioritised portfolio of antibiotics. Use of these tools or demonstration of other strong forecasting methods may become prerequisites to receiving catalytic financing or other SECURE support.
- Financial risks for the mechanism are substantial once the models scale up as additional countries are added. There is also a risk that countries don't buy the products for which supplier guarantees are provided. These financial risks will need to be mitigated by a guarantor stepping in to pay. SECURE will need to source suitable financial backers and donors to support the establishment of the mechanism including existing and emerging regional development banks.

Key takeaways and next steps for SECURE

SECURE can play a key role in improving access to appropriate essential antibiotics. Three packages of interventions tailored to key access issues of common drug archetypes were deemed feasible and provide a very promising financial case to begin SECURE's implementation. Savings were shown for countries as compared to their average cost baselines, while the cost to create the mechanism with an existing procurement entity is considered both reasonable and sustainable compared to other scenarios tested. LMICs may not find it feasible to agree to upfront supplier guarantees for Reserve antibiotics given the low historical demand for these products and often limited drug budgets. Such models may be tried as innovative pilots with interested countries once the SECURE mechanism is functional with proven benefits.

It is important to note that SECURE will work in partnership with organizations and countries to encourage their solidarity. Stakeholders supported the use of existing international or regional pooled procurement entities. The selection of the right entity or entities will be crucial to SECURE's success.

It is envisioned that, in collaboration with countries, a small portfolio of "Access", "Watch", and "Reserve" antibiotics will be identified by early 2024 to test the SECURE model. The products which will be selected will have strong public health importance coupled with persistent access challenges, widely applicable to many countries. Impacts and costs will be modelled. This more concrete and granular data will facilitate discussions with potential partners in the implementation phase, including participating countries.

SECURE can support countries with additional interventions to optimize their access antibiotic portfolios, improve market intelligence and more reliable forecasting models and can advocate for national regulatory authorities to address shortages.

Determining the most practical stewardship levers which can be included within the SECURE interventions will go hand in hand with the portfolio decisions and require a country-specific lens.

In the next phase of SECURE, regional and country discussions will aim to tailor and combine the economic and procurement tools with the broader SECURE interventions to address individual product and country needs.

Acknowledgements

GARDP would like to acknowledge the Boston Consulting Group for its contribution to the development of the economic and procurement tools. We acknowledge that specific assumptions have been adjusted since engaging the BCG team, for the purpose of the scope of this report.

We would also like to thank all partner organisations and key opinion holders and stakeholders for their expertise and insights into the development of this model as well as the key lessons learnt. We look forward to working with you more closely in the future to implement these solutions in countries where access is a challenge.
Please see annexure A for all key stakeholders involved.

Finally, we are very grateful for the contributions of our donors: Public Health Agency of Canada (PHAC), Health Emergency Preparedness and Response Authority (HERA), Swiss Agency for Development and Corporation (SDC) and Wellcome.

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Approach to determine potential suitable economic and procurement tools for SECURE

SECURE is an innovative initiative being developed by the World Health Organization (WHO) and the Global Antibiotic Research and Development Partnership (GARDP) to improve access to both existing and new antibiotics.

SECURE will increase access to a portfolio of quality-assured antibiotics in a sustainable, equitable and appropriate way. It will improve appropriate access to both existing and new antibiotics. SECURE's antibiotic portfolio will be adapted to meet national public health and clinical needs.

A key aim of SECURE is to address access barriers by creating market efficiencies and predictability, for example by aggregating antibiotic demand across multiple countries through pooled or coordinated procurement mechanisms. A further aim is to optimize pricing and availability for countries by creating a more attractive market for suppliers, while ensuring appropriate stewardship.

Under the guidance of key stakeholders, and work done by both GARDP and WHO with the support from Boston Consulting Group, an analysis was undertaken to model the impact and costs of different economic and procurement tools that could be undertaken as part of the SECURE initiative to meet the above aims.

The following approach was taken to identify a suitable package of economic and procurement tools for SECURE:

- Understanding the key challenges for LMICs in accessing antibiotics
- Identifying potential economic and procurement tools to implement via SECURE to improve access
- Testing the identified tools through modelled scenarios to identify those with highest potential

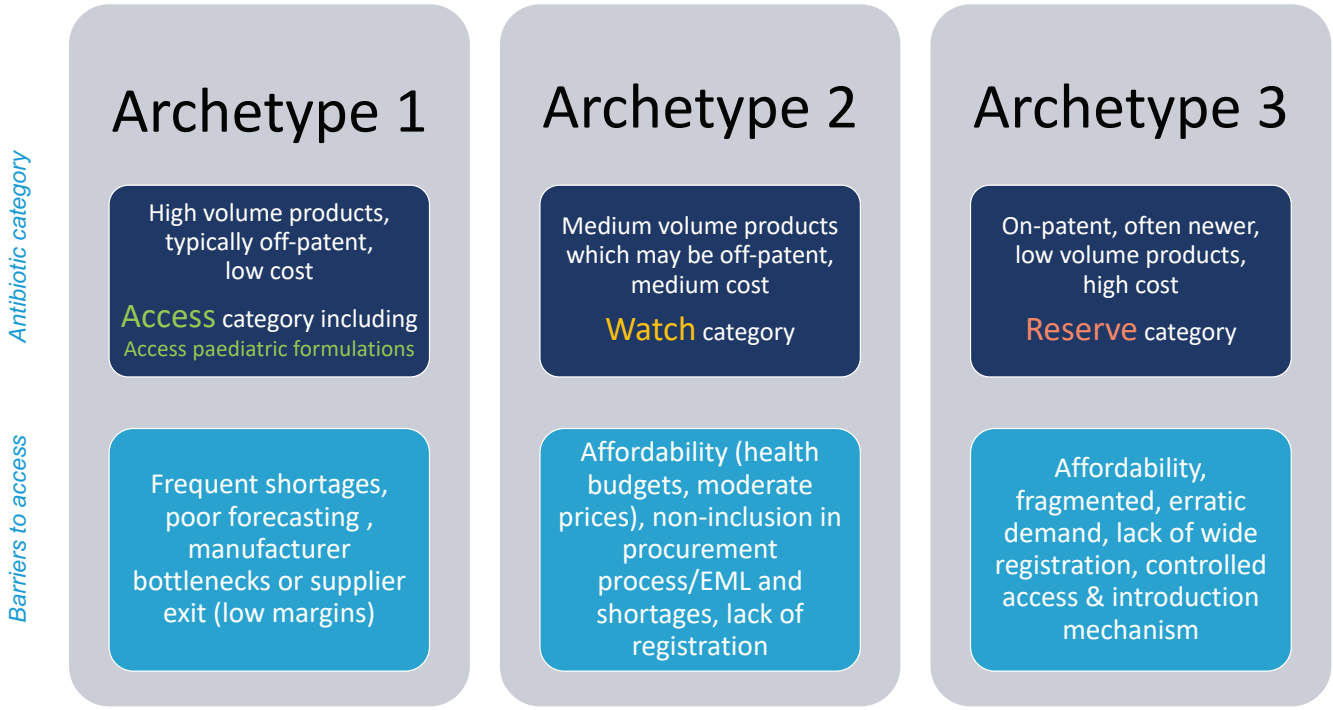
Key access challenges for antibiotics for LMICs

Based on an analysis that included stakeholder assessments and market intelligence (secondary data), three 'antibiotic archetypes', based on the WHO AWaRe classification of antibiotics, were identified along with their associated key access[3] challenges that could be addressed by SECURE (see Figure 1 overleaf):

- **Archetype 1: High volume, off-patent antibiotics characterized by low margins. These antibiotics were often in the "Access" category.** Recurrent shortages stemming from inaccurate forecasting manufacturing constraints, or suppliers ceasing production, leaving a vulnerable supply or unserved geographies, were identified as the most significant barriers.
- **Archetype 2: Antibiotics that are of medium volume, on or off patent. These antibiotics were often classified under the "Watch" category**. Challenges to access include factors such as cost considerations relative to national budgets, omission from procurement policies, and frequent product shortages.
- **Archetype 3: On-patent, recently introduced, low volume highly priced products. These antibiotics are typically Reserve or lower-volume Watch antibiotics.** Key challenges hindering access to these products involve prices, financial constraints and inconsistent and segmented demand, leading to limited registration across essential geographical areas.

3 Access is defined by the World Health Assembly as the reliable and consistent availability of appropriate essential, quality medicines at health facilities, the rational prescribing and dispensing of such medicines and ensuring that they are affordable.

Figure 1 *Antibiotic Archetypes and their associated barriers to access*



Sample antibiotics analysed

One sample antibiotic was chosen (based on data availability) to model the costs to SECURE and potential price reductions and country savings in each scenario. Antibiotics included in the scenarios were selected from the WHO Essential Medicines List (EML), based on the availability of price and volume data estimates (available from a representative LMIC). The use of these drugs in the analysis has no bearing on the selection of drugs for the SECURE portfolio.

Archetype 1, High-volume products, typically off-patent:

- Sample antibiotic: amoxicillin 500mg capsule – Access
- Second Sample antibiotic: amoxicillin 250mg/5ml, oral solution, 100 ml for paediatrics – Access

Archetype 2, Medium-volume products, possibly off-patent:

- Sample antibiotic: ceftriaxone; 1g; injection parenteral – Watch

Archetype 3, On-patent, typically recently introduced, newer, low volume products usually highly priced:

- Sample antibiotic: ceftazidime-avibactam, 2.5 grams parenteral - Reserve

Sample country assumptions

The initial analysis was focused on low- and middle-income countries (LMICs), with the assumption that high-income countries (HICs) may be modelled and included later.

The analysis focused on a small country, with a total population of 12 million, of which 75% (9.3 million) rely on public sector health services. This country was added into a pooled procurement mechanism with an assumed

pool of 100 million public sector population. Tunisia was selected as the small country for modelling purposes due to availability of data for the required variables. One sample antibiotic was chosen to represent each archetype in order to use real pricing data to model. Public sector tender prices as well as estimates for consumption volumes for sample antibiotics were available from a representative country to assist in the modelling. This is why the 100 million pool was modelled on the public sector population only.

As the model is adaptable, other countries can be chosen apart from Tunisia to see how the SECURE mechanism influences their costs and savings. Each country needs to be categorized based on its population size as the assumption on average drug price currently paid will depend on country size and economic level.

Identification of the most suitable economic and procurement tools

Identifying the most suitable economic and procurement tools was based on some assumptions on tools that have shown promise in the past with other essential medicines. This menu of tools was reviewed to assess the potential impact on the specific access challenges experienced by LMICs and their economic context.

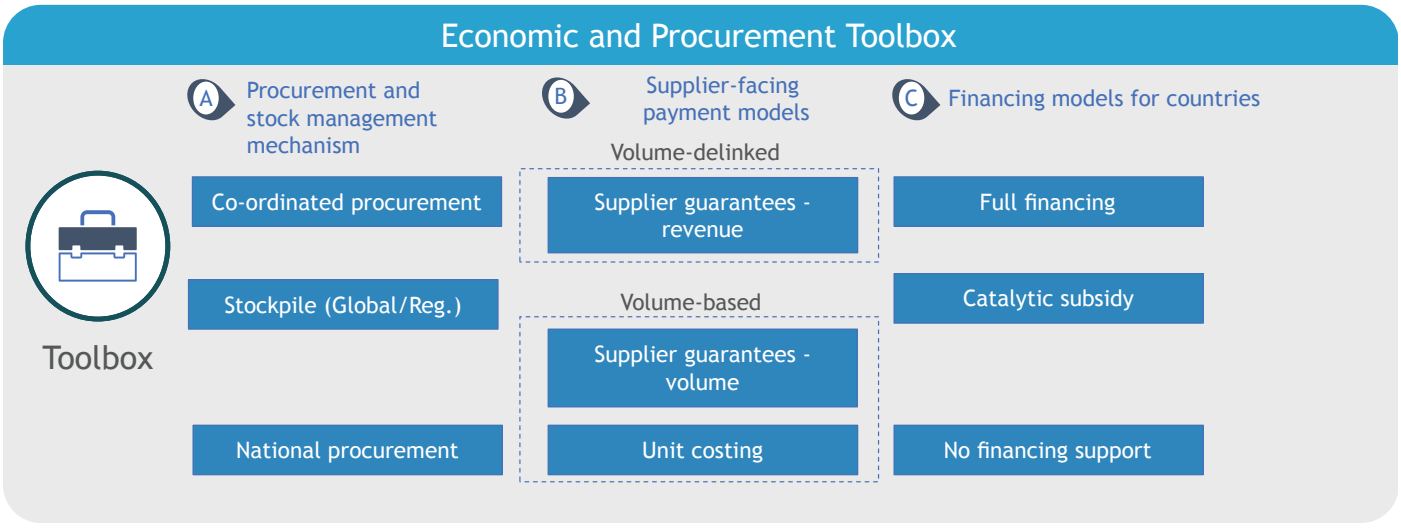
Economic and procurement toolkit components

Within the toolkit are various procurement and economic tools. Specific tools within the toolkit were identified as suitable. These were then modelled against the antibiotic archetypes. These tools are described below.

Tools tested included:

- Pooled/co-ordinated procurement
- National procurement by the countries
- Stockpiling options included stand-alone rotating stockpiles and revolving stockpiles linked to a pooled procurement mechanism
- Country financing support ranging from no to minimal or more substantial catalytic financing including full financing
- Supplier guarantees including revenue and volume guarantees [4]
- Unit costing of product at base price

Figure 2 *Economic and procurement toolbox tested for SECURE*



4 Stakeholders interviewed suggested that subscription models, which are structured to provide a pull incentive for antibiotic Research and Development (R&D), are not appropriate for LMICs and therefore these were not modelled

Procurement and Stock management

Coordinated procurement options included informed coordinated buying whereby entities share market research and other data, but contract and buy separately; joint contracting in which multiple entities negotiate prices together but purchase independently; and pooled procurement with central contracting and purchasing where multiple entities purchase antibiotics together to cover their needs in a coordinated way.

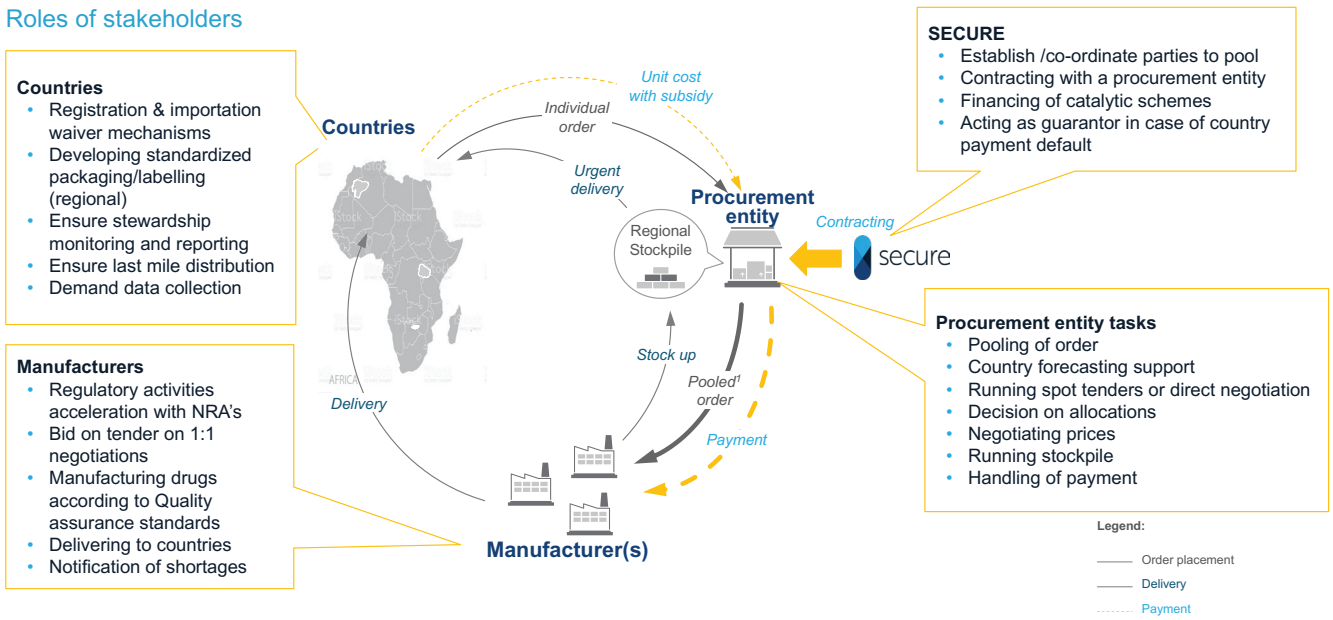
The assumption is that SECURE would contract with an existing procurement service agent (PSA) or agents (including existing regional pooled procurement entities) and pay a service fee. The PSA would provide services to support country forecasting, pooling of orders, and contracting with suppliers on price and terms. It would also involve running tenders or direct negotiations on prices; decisions on allocations; ordering and payments; supply and logistics with warehouses containing the stockpiles; and transportation to the ports of entry of countries. Thereafter the model assumes that the country would take control of the last mile processes of distribution.

Countries in the mechanism individually place orders for antibiotics via the PSA. Payment of the order is made directly to the PSA. In case of acute shortages, countries are able to order a direct delivery via the stockpile. The manufacturer ships orders directly to countries except for a portion which goes through the warehouse to rotate or replenish stock.

Expert interviews and other global health stakeholders have generally indicated that pooled procurement can improve access, through:

1. **Price reductions:** potentially up to 20-30% or higher reductions in price over 5 years[5]
2. **Increase in supplier diversity:** Over a period of 5 years a steady increase in number of quality-assured vendors across product categories resulting in a diversity of suppliers and increase sustainability of supply[6]

Figure 3 *Pooled procurement and stock management mechanism illustration*



5 Source: Past BCG global health casework, Organization of Eastern Caribbean States Pharmaceutical Procurement Services with volume, Management Sciences for Health; expert interviews; BCG analysis

6 Past BCG casework

Stockpiles: Options examined include rotating stockpiles with annual replenishments or revolving with continuous resupply and replacements as drugs are used by countries. These could be managed regionally or globally and payment to the manufacturer would be on consignment (i.e. when drug is delivered) or upfront. In the case of a revolving stockpile, the stockpile would be managed by the pooled procurement entity.

In the case of a revolving stockpile, a certain share of total volume procured will go to a warehouse to seed a rotating stockpile. The rest of the volume, which covers regular expected demand, will go to countries.

The model assumed that a revolving stockpile is seeded in year 1. The drugs have three years of shelf life, disbursed with one year left. From the regularly pooled procured volume, a share will always go to the warehouse to replenish the stockpile (which is maintained at constant levels of 25% of pool demand).

SECURE would pay the warehousing (30% of inventory value) and transportation costs (5% of order value), as well as any additional operating expenses (2.5-3%) to manage the stockpile. The stockpile will provide a backstop source of supply in case of forecasting errors, surges, or other factors leading to shortages.

Supplier guarantees

Several "supplier-facing" financing options were identified. The goal of the models, in particular the volume de-linked or partially de-linked models is to improve supplier predictability, create economies of scale, and reduce risk for suppliers while securing access including through improved leverage to negotiate prices and/or registration in high-burden geographies. Delinking volumes from revenues would reduce the incentives to increase sales of the product whilst still allowing the manufacturer to recoup some of the costs of research and development by maintaining higher prices in high incomes countries.

We evaluated two models: Revenue guarantee and Volume guarantee[7]:

- **Revenue guarantee:** In a revenue guarantee model, a supplier is guaranteed an annual revenue for supplying product based on the needs of the country. The guarantee is set at a level that ensures a viable business case for the supplier. It is anticipated that the revenue guarantee will result in the country overpaying for the product as volumes needed will be (initially) lower than the revenue amount. Should the demand exceed the revenue guarantee, then it will be paid for at a unit cost at the agreed price.
  The structure and level of the guarantee used in this analysis was modelled on the Sweden model[8] and adjusted for the average LMIC product price to USD 400,000 per annum for a demand of a population of the small LMIC modelled for this exercise (volume of 4071 Standard Units per annum)
- **Volume guarantee:** A minimum volume is guaranteed to the manufacturer (at an agreed price), to ensure a minimum scale for production for the manufacturer. Such a guarantee is often used to accelerate production, broaden product registration and/or secure a lower price especially for small scale manufacturers where there is uncertainty about actual demand. Technically the physical exchange of the product is anticipated and can be matched to the volume guaranteed. If the demand is higher than the guaranteed volume, then it will be paid on a per-unit basis. The guarantee used in this analysis was based upon 4071 standard units (SU) modelled based on the average LMIC historical demand (331 SU's per 1 million population per annum)
  Both volume and revenue guarantees incentivize the manufacturer to allocate manufacturing capacity to service the pool. Due to the guarantee and large pooled volume, the manufacturer provides a competitive price for purchases through the mechanism.

7 The definitions provided were the projects working definitions

8 Sweden model: Public Health Agency of Sweden (PHAS) pilot model for keeping approved antibiotics available on the Swedish market (2018) via a revenue guarantee of 430k EUR.

Unit costing

Unit costing as a volume-based option was used as the default option in case none of the above arrangements was applicable as it would allow countries outside of the pool to participate.

Flexibility was built into some scenarios to allow countries which didn't want to join the pooled procurement process to still benefit from the mechanism (either purchasing directly at manufacturer with SECURE discount or only accessing the stockpile in case of shortages). The following assumptions were included:

- *Direct purchasing at manufacturer (no pool participation) Reserve antibiotics*
    - For a country not participating in the pooled procurement mechanism there is an option to directly purchase at the manufacturer with SECURE negotiated discount. However, the country must pay an additional 5% fee on the purchase and cannot benefit from the product subsidy scheme through SECURE.
- *Direct purchase from stockpile (no pool participation) Watch or Access antibiotics*
    - For a country not participating in the pooled procurement mechanism there is an option to only access the stockpile in case of shortages. However, the country must pay an additional 5% fee on the purchase via the pooled discount price negotiated by SECURE.

Financing tools for countries

Various financing options were identified.

- **Time-limited catalytic financing**: For certain higher cost products, a time limited subsidy was included to offset initial higher prices and enable countries to participate in the pool. With increasing demand and corresponding lower prices, it is envisaged that the subsidy could decrease over time. The following assumptions were included in the model:
    - Option for higher priced Reserve antibiotics: SECURE subsidises 95% of the cost for drugs in year 1 and year 2; 79% in year 3, declining thereafter at a rate of 5% per annum[9]
    - Option for higher priced Reserve antibiotics where there is a single country participating in a revenue guarantee: SECURE subsidises 50% of the revenue guarantee. If the country exceeds the ceiling volume specified in the revenue guarantee, then the country purchases on a per-unit basis
    - Option for medium-priced Watch antibiotics: SECURE subsidises 25% of cost for drugs in year 1, reducing incrementally to 5% in year 5 and then continues as a self-financing scheme thereafter
- **Full financing** through SECURE was modelled as an alternative for high volume, low price Access antibiotics.
- **No financing support** was an option in case of antibiotics that were already registered, were low priced and high volume. The assumption underlying this option is that countries are already purchasing those drugs, just not at the full demand, and the pooled procurement mechanism would provide enough discount to offset affordability issues to a degree where demand is covered, and no further financing support would be needed.

9 This was modelled based on the GAVI model of country financing, however there was a time limit in years to the financing rather than a graduation out following economic status of country

Other financial assumptions

- Warehouse costs amount to 30% of inventory (stockpile) value, based on benchmarks. The purchase cadence is set at two orders annually, and 25% of normal stock passes through the warehouse for rotational purposes, which is the share of regular supply that needs to be processed.
- Transportation costs are 5% of order value (included in subsidy), shown in the model but not added as incremental costs. Import duties are set at 0% due to the assumption of countries providing import duty waivers (likely varies by country).
- Additional operating expenses for the stockpile are assumed to be 2.5% or 3%[10] of stockpile value.

Tools considered however not modelled

Subscription model: Subscriptions models were not tested in our modelling as stakeholders indicated that the goal of the current examples of subscription models is to provide a pull incentive for R&D alongside enabling access. In such models, buyers provide a fixed total price (regardless of the volume of demand) to pharmaceutical companies for a set period of years in return for a guaranteed unlimited access to the antibiotic rather than relying purely on a price per pill. The value of the payment for the product is "delinked" from the actual volume of product provided and represents an "insurance value" for society. Stakeholders suggested that both the complexity of determining the value of an antibiotic to set a subscription price and the increased cost to the countries of such a mechanism would likely be unattractive as an initial LMIC pilot for SECURE.

Other country financing may take the form of a grant to support country activities during the period of new product introduction where additional new processes need to be established, including stewardship.

Drug prices and demand assumptions

Drug price data for individual antibiotics and formulations/strengths vary by country size, income level and availability of pricing information. A conservative approach was taken:

a. Data sources included Global Data.com database and IQVIA data and a mid-sized LMIC[11]

b. For each drug (specific formulation and strength) a starting or "base" price (pre-intervention) was determined using the average published tender prices, weighted by volumes, from a mid-sized LMIC.

c. The base price for Access and Watch antibiotics was converted to a price per daily dose and kept as an average price per unit for the Reserve antibiotics. The model was therefore able to match demand volumes in daily doses (for the Access and Watch) or SKU's (for Reserve) to the correct price unit in the data source.

d. The model assumes at baseline (without SECURE) that a medium sized LMIC country pays the average drug base price. A smaller country is assumed to pay a slightly higher price due to lower purchase volumes before the mechanism and larger countries are assumed to start off at a lower price than medium/small countries.

   i. Small (<25 million public patients) paying 110% of the average base price
   ii. Medium (25-100 million public patients) paying 100% of the average base price and
   iii. Large (>100 million public patients) pay 80% of the average base price

10 Based on PSA fees: Global Fund and i+Solutions

11 South Africa was the primary source

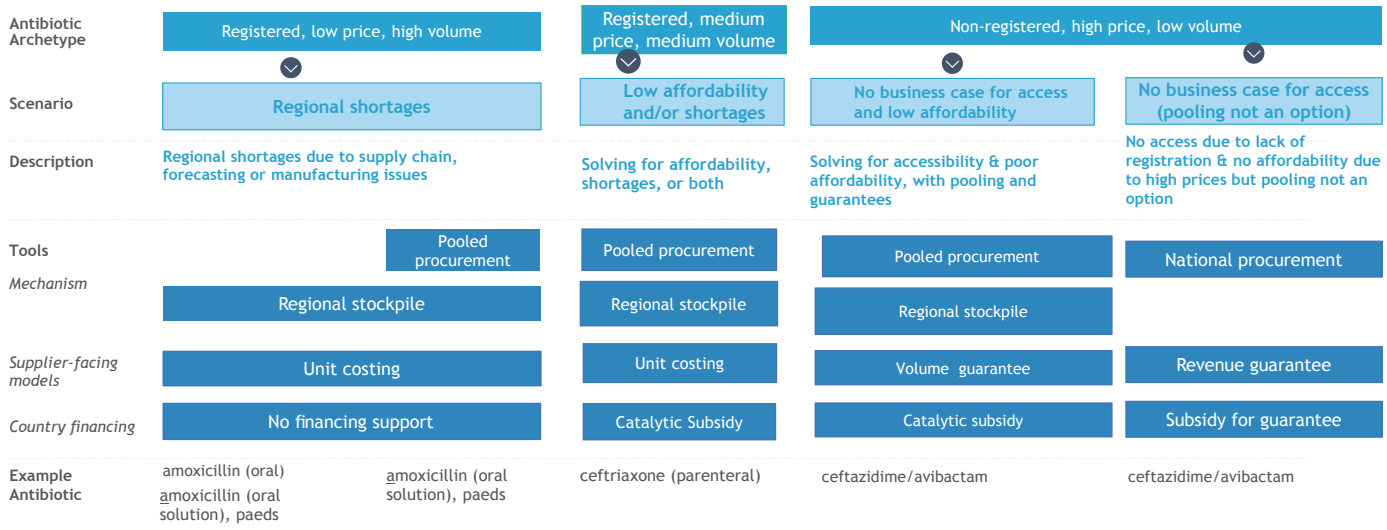
e. Given these assumptions, the price reduction through the pooled procurement mechanism leads to larger countries receiving a smaller overall price reduction (already lower starting point) and small countries receiving a larger price reduction (already higher starting point).

f. The potential demand volumes was based upon published data (Access and Watch antibiotics) from WHO GLASS[12] and the South African Antimicrobial Resistance Reports[13] and population-indexed demand for a range of LMICs for Reserve antibiotics (using IQVIA data). The increase in demand for the pool of countries was modelled to reach the average defined daily dose per 1 million population by year 5.

Testing the economic and procurement tools for feasibility and suitability

For each antibiotic archetype, various combinations of economic and procurement tools were modelled and those which could help to address key access barriers most feasibly were identified This resulted in a set of six scenarios being defined and tested through the model (see figure 4 below).

Figure 4 *Antibiotic Archetypes and Barriers to access with economic and procurement tools to support access as modelled*



Scenario 1 and 2: Access – Stand-alone stockpile

Antibiotic archetype: High-volume, low price products, typically off-patent.

Exemplar drugs:

a) amoxicillin 500mg capsule – (Access)

b) amoxicillin 250mg/5ml, oral solution, 100 ml for paediatrics (Access)

Access barriers: Regional shortages due to supply chain, forecasting or manufacturers issues

Tools tested:

i. Stockpiling strategy: Stand-alone rotating stockpile, maintained at constant levels, (25% or 3 months supply) of expected pool demand and annually replenished. The drugs have 3 years of shelf life and are disbursed with 1 year left.

12 WHO GLASS – World Health Organisation Global Antimicrobial Resistance and Use Surveillance System

13 https://knowledgehub.health.gov.za/system/files/elibdownloads/2023.04/AMR%2520and%2520AMC%2520report%2520for%25202021%2520in%2520South%2520African_June2022.pdf

ii. Supplier payment model: Unit costing
iii. Country financing model: No subsidy

Scenario 3: Access – Pooled procurement with stockpile

Antibiotic archetype: High-volume, low price products, typically off-patent

Exemplar drugs:

a) amoxicillin 250mg/5ml, oral solution, 100 ml for paediatrics (Access)

Access barriers: Regional shortages due to supply chain, forecasting or manufacturers issues. Affordability of quality-assured paediatric formulations.

Tools tested:

a) Procurement mechanism: Pooled procurement with multiple vendors
b) Stockpiling strategy: Revolving stockpile linked to the pooled procurement mechanism to protect against shortages or unpredicted outbreaks at regional or global level
c) Supplier payment model: Unit costing
d) Country financing model: No country financing

Scenario 4: Watch – Pooled procurement with stockpile and minimal catalytic financing

Antibiotic archetype: Medium-volume products, possibly off-patent:

Exemplar drug:

a) ceftriaxone; 1g; injection parenteral (Watch)

Access barriers: Regional shortages due to supply chain, forecasting or manufacturers issues. Affordability of quality-assured Watch drugs or paediatric formulations.

Tools tested:

a) Procurement mechanism: Pooled procurement with multiple vendors
b) Stockpiling strategy: Revolving stockpile linked to the pooled procurement mechanism to protect against shortages or unpredicted outbreaks at regional or global level
c) Supplier payment model: Unit costing
d) Country financing model: Catalytic subsidy as an option for higher priced Watch antibiotics. SECURE subsidises 25% of cost for drugs in year 1, reducing incrementally to 5% in year 5 and then continues as a self-financing scheme thereafter
e) Flexibility: an option where some countries did not participate in the pooled procurement mechanism but can leverage the framework agreement and buy directly from the suppliers

Scenario 5: Reserve – Pooled procurement, stockpile, volume guarantee and catalytic financing

Antibiotic archetype: High priced, low-volume product, not registered in country

Exemplar drug :

f) ceftazadime-avibactam 2.5 grams parenteral – Reserve

Access barriers: Affordability, limited registration, single supplier (in some cases), limited business case for supplier to enter into low-volume, unpredictable fragmented markets.

Intervention components included in the model tested:

g) Procurement mechanism: Pooled procurement

h) Stockpiling strategy: Revolving stockpile linked to the pooled procurement mechanism to mitigate against poor forecasting, emergency order placement, shortages or unpredicted outbreaks at regional or global level

i) Supplier payment model: Supplier volume guarantee - The guarantee was based on about 4,071 standard units (SU) of product (equal to a revenue of about USD 150k[14]). The demand increased incrementally from 10% to 100% in year 5 of the anticipated average LMIC demand for the pool.

j) Country financing model: Catalytic subsidy: SECURE subsidises 95% of the cost for drugs in year 1 and year 2; 79% in year 3 and thereafter a decline of 5% per annum

k) Flexibility - included an option where some countries did not participate in the pooled procurement mechanism but can leverage the framework agreement and buy directly from the suppliers.

Scenario 6: Reserve – Single country revenue guarantee

Antibiotic archetype: Antibiotic archetype: High priced, low-volume product, not registered in country

Exemplar drug :

l) ceftazadime-avibactam 2.5 grams parenteral – Reserve

Access barriers: Affordability, limited registration, single supplier (in some cases), limited business case for supplier to enter into low-volume, unpredictable fragmented markets. In addition, the country cannot/doesn't want to participate in pooling mechanism, and drug prices are too high to be affordable for the country.

Intervention components included in the model tested:

i. Procurement mechanism: Direct procurement by the countries own procurement entity.

ii. Supplier payment model: Supplier revenue guarantee - The revenue guarantee was based on a revenue of USD 400[15]. SECURE subsidy covers 50% of the payment of the guarantee for the duration of the contract. The demand increased incrementally from 10% to 75% in year 5 of the anticipated average LMIC demand.

iii. Country financing model: no additional subsidy

14 Assumption is that the average LMIC volumes of SU's is multiplied by the discounted LMIC price of USD 36.74 and is dependent on agreement by supplier

15 Assumption is that the average LMIC volumes of SU's is multiplied by the average LMIC price of USD 96.68 and is dependent on agreement by supplier

Conditions necessary for the models

Testing and comparing outputs across different scenarios was only possible by standardising and adding conditions for each model to work. These conditions are critical to achieve the desired impact when implemented.

Some of these conditions include:

- The willingness of countries and manufacturers to adopt pooled procurement using an existing procurement entity contracted by SECURE
- Establishing mechanisms to implement stewardship, availability of diagnostics for laboratory sensitivity testing and monitoring systems for pharmacovigilance
- Mechanisms to accelerate or harmonize drug registration processes of selected prioritized products across a range of countries including the development of standardized packaging/labelling
- The existence of a functional in-country distribution and cold chain (where needed) to ensure the drugs reach the patients

Outputs for each scenario

The model tested a range of outputs including:

- Country product price reductions and total savings resulting from the package of tools applied. These reflect the difference between the product price they would have paid using the counterfactual of the status quo price (based on LMIC average base price paid) and the price with the discounts from the pooling mechanisms as well as from the economic tools applied under different scenarios
- Costs to SECURE, including service fee for the administrative processes of the procurement mechanism, financing of the country subsidy mechanisms, guarantees to the suppliers, costs of the administration of the procurement entity as well as the warehousing and stockpiling costs associated
- Benefits looks at the impact of the procurement mechanism in relation to the benefits to the country to access the antibiotics and suppliers
- Risks are aspects that would need to be mitigated or could cause the mechanism to fail

Overview of outcomes of all Scenarios

- The figure below summarizes the outcomes of each scenario over the 5 years modelled in terms of country savings and SECURE costs to support the mechanism. Results are shown in terms of overall cost savings to those participating in pooling (for the total 100 million population pool), potential product price reductions, and estimated cost of implementing the contracting of the mechanism to a procurement entity over the initial 5 years. All scenarios are described below in more detail.

Figure 5 *Summary of outputs for all Scenarios*

Antibiotic Archetype	Tools	Antibiotic example (single drug per archetype)	Pooled Country savings over 5 yrs[1]	% price reduction potential[2]	Costs of mechanism over 5 yrs[3]
1. Registered, low price, high volume	Pooled procurement + revolving Stockpile	"Access" antibiotic (amoxycillin oral solution)	USD 4.15 million	16%	USD 3.2 million
2. Registered, medium price, medium volume	Pooled procurement + revolving stockpile + with catalytic subsidy	"Watch" parenteral antibiotic (ceftriaxone IV) (subsidy applied at 25% and declining thereafter)	USD 7.68 million	37%	USD 5.78 million
3. Non-registered, high price, low volume	Pooled procurement + revolving stockpile + supplier guarantee + catalytic subsidy	"Reserve" antibiotic (ceftazidime/avibactam IV) (subsidy applied at 95% and declining thereafter)	USD 8.86 million	>80%	USD 3.64 million + USD *0.748* million[4]

[1] Savings calculated at average LMIC price for a small country (e.g., Tunisia) for an individual antibiotic and summed up for the entire 100 million population pool

[2] Discount based on average LMIC price for antibiotic

[3] Mechanism includes contracting with an existing Procurement Entity – service fees, stockpile, warehousing and wastage costs

[4] SECURE guarantee liability should one be included for the countries in the pool

Outcomes of Scenario 1 and 2: Access – Stand-alone stockpile

To address shortages with a stand-alone rotating stockpile for selected Access antibiotics.

Antibiotic archetype: High-volume, low price products, typically off-patent.

Exemplar drugs:

a. amoxicillin 500mg capsule – (Access)

b. amoxicillin 250mg/5ml, oral solution, 100 ml for paediatrics (Access)

Tools	
Mechanism	Regional rotating stockpile
Supplier-facing models	Unit costing
Country financing	No financing support

Scenario 1: Access – Stand-alone stockpile Adult formulation

SECURE Costs for Mechanism

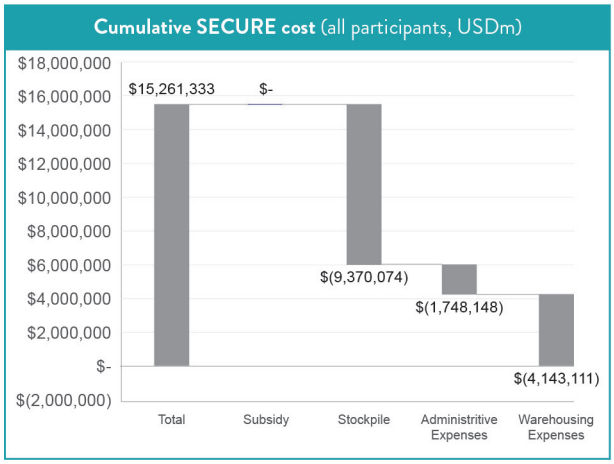
The costs to run such a rotating stockpile were estimated at USD 15.3 million for 5 years for a single product (modelled on amoxicillin 500mg capsule) for a pool of 100 million population. This includes warehousing expenses (USD 4.14 million), stockpile costs (USD 9.37 million), unused stock USD 1.54 million and administrative expenses for running the mechanism (USD 1.75 million). This is not likely to be economically feasible or effective, as the choice of stockpile size will depend on the severity of expected shortages and the ability to predict which antibiotics and which countries may be prone to shortages, so that the stockpile can be placed in the correct region.

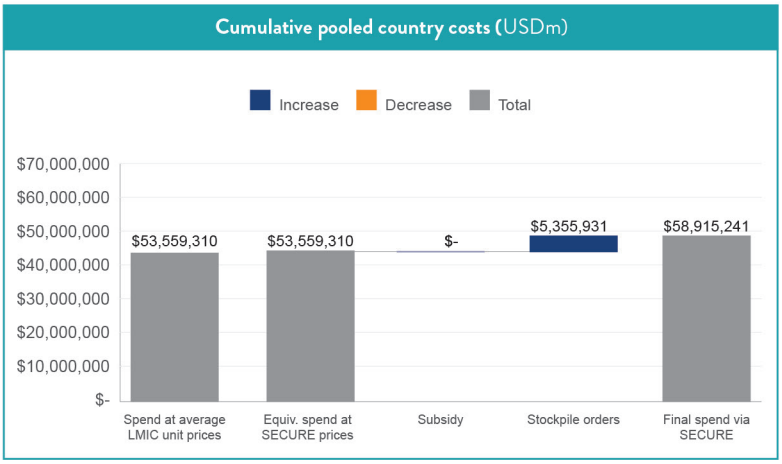
Country Pool Costs

Given the fact that this scenario covers unanticipated country demand, the cost to the country only increases through stockpile orders without any savings for the country (no subsidy or other form of discount from pooling). Over 5 years, baseline spend for all countries in the pool will therefore shift from a baseline of USD 53.6 million to USD 58.9 million (USD 0.643 million in incremental costs) to create and utilise such a stockpile - an additional 10% on the base cost of the drug.

Figure 6 *Outputs of Scenario 1: Access - Stand-alone stockpile Adult formulation*

Key scenario outcomes | **Antibiotic:** Low price, high volume, registered | amoxicillin





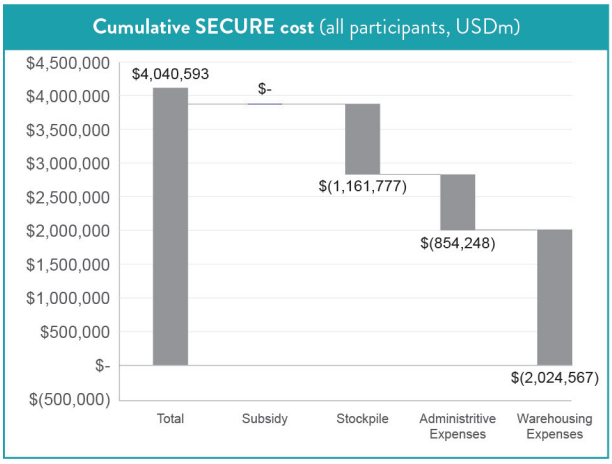
Scenario 2: Access – Stand-alone stockpile Paediatric oral solution

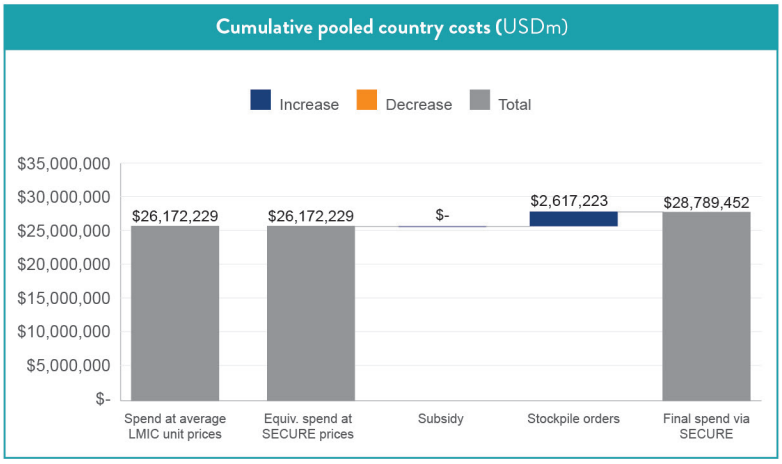
The scenario was modelled on amoxicillin 250mg/5ml, oral solution, 100 ml for paediatrics which is a low-price product with half the volumes of amoxicillin capsules. Given the lower volumes some of the associated operational costs were therefore lower. The total costs to SECURE over 5 years amounts to USD 4.04 million with reductions in the stockpile costs (USD 1.16 million), administrative expenses (USD 0.854 million) and warehousing expenses (USD 2.02 million) when compared to scenario 1.

Total cost for all countries in the pool will therefore shift from a baseline of USD 26.17 million to USD 28.789 million (USD 2.617 million in incremental costs) to create and utilise such a stockpile (a 10% increase).

Figure 7 *Outputs of Scenario 2- Stand-alone stockpile – Paediatric oral solution*

Key scenario outcomes | **Antibiotic:** Low price, high volume, registered | amoxicillin oral solutions paeds





Alternative options to reduce costs to SECURE and countries

Another option to reduce the costs to SECURE would be to reduce the size of the stockpile by half. This would reduce SECURE's costs by 40% and the countries' cost would reduce by 4,5%. Modelling a smaller stockpile and lower consumption results in a lower cost estimate, but may not be sufficient if countries encounter a simultaneous demand surge or are dependant on the same supplier that is experiencing a shortage.

This comes with the risk that in a significant shortage, where countries within a region are simultaneously affected, the demand required from the stockpile might exceed the stock available, thus limiting access.

Additionally, reducing stockpile size may have some minor additional volumetric effects on pricing (not modelled).

And finally, another alternative is scenario 3 which is a pooled procurement mechanism alongside a revolving stockpile to protect against shortages (overleaf).

Outcomes of Scenario 3: Access – Pooled procurement with stockpile

To address access issues for selected Access paediatric formulations using pooling and a revolving stockpile.

Antibiotic archetype: High-volume, low price products, typically off-patent.

Exemplar drug:

a. amoxicillin 250mg/5ml, oral solution, 100 ml for paediatrics (Access)

Tools	Pooled procurement
Mechanism	Regional revolving stockpile
Supplier-facing models	Unit costing
Country financing	No financing support

SECURE Costs for Mechanism

The costs to run such a mechanism would be USD 3.2 million over 5 years for a single product (modelled on amoxicillin 250mg/5ml, oral solution, 100 ml for paediatrics) for the pool of 100 million.

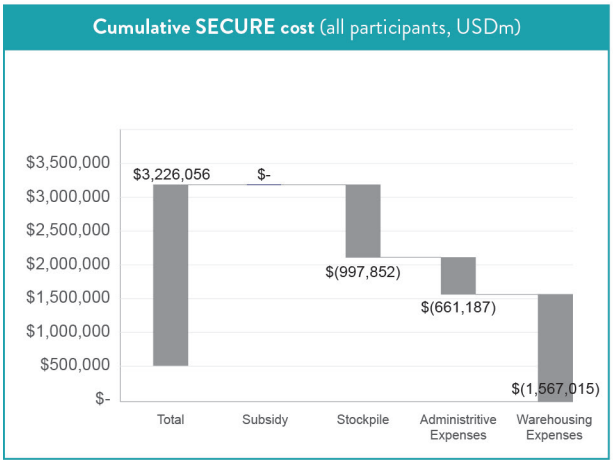
Costs include stockpile costs (USD 0.998 million) warehousing expenses (USD 1.57 million), and administrative costs (USD 0.66 million).

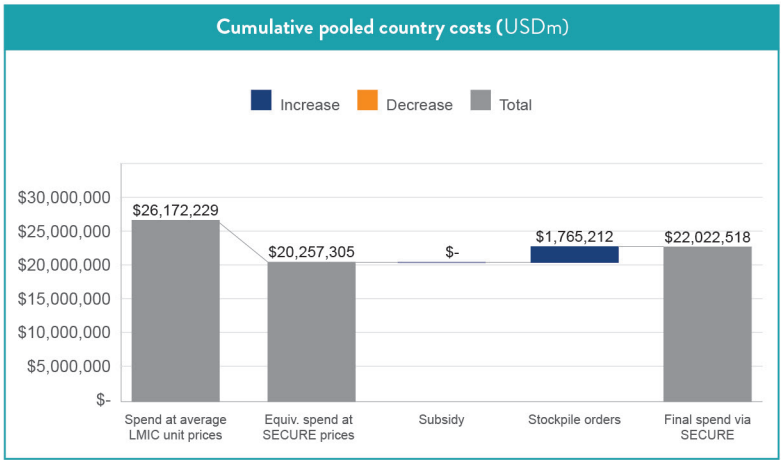
Country Costs and Savings

This mechanism would enable countries participating to save approximately 15.8% - USD 4.15 million for the entire pool. These savings come from pooling (USD 2.617 million), long term contracting benefits (USD 3.3 million) with a slight incremental cost of USD 1.77 million for stockpile orders.

Figure 8 *Outputs for Scenario 3 – Access – Pooled procurement with stockpile*

Key scenario outcomes | **Antibiotic:** Low price, high volume, registered | amoxicillin oral solution





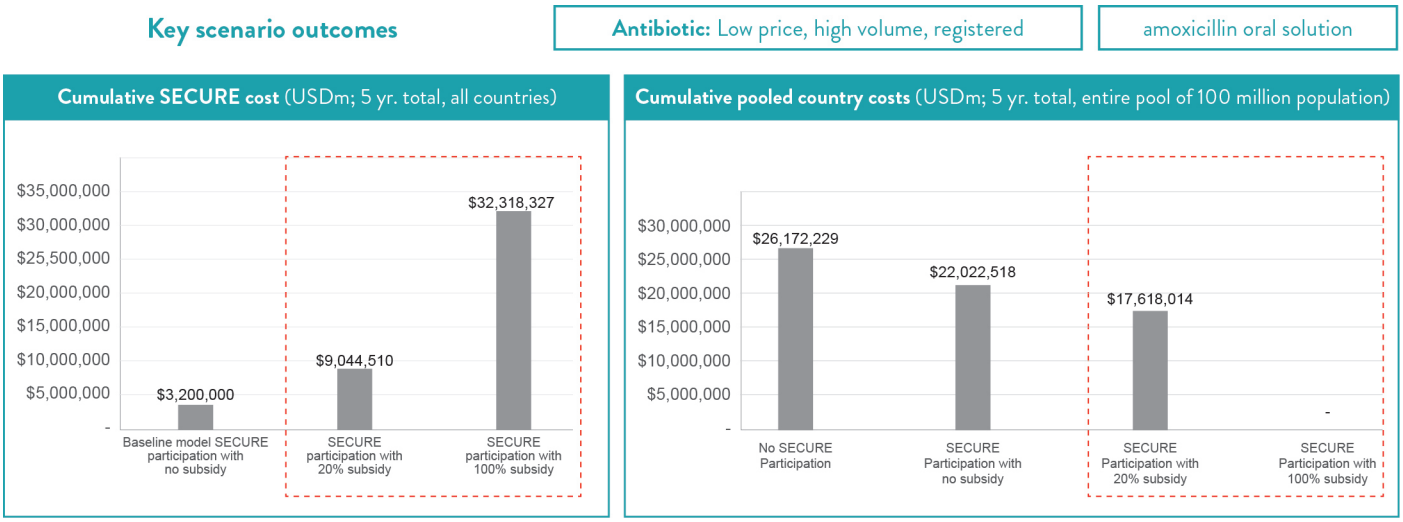
Alternative options to address affordability in Low Income Countries

The model was run testing various levels of subsidy for countries with a 20% and full financing scenario (100% subsidy) modelled. In the 20% subsidy scenarios, the costs to SECURE would increase from USD 3.2 million to USD 9.044 million whilst bringing down the costs of the product for the entire pool of countries from USD 22.02 million to USD 17.6 million over the 5 years. A 100% subsidy would cost SECURE USD 32.3 million and effectively make the products free to the pool of countries.

Fulll financing through SECURE places a heavy reliance on ongoing external financing and does not support country self-sufficiency in providing access to basic antibiotics as part of universal health coverage.

However, if funding is available SECURE could consider supporting very vulnerable countries for pandemic preparedness and for public health needs, where access to a basket of quality assured Access antibiotics would be life-saving, especially for neonates and children.

Figure 9 *Outputs for alternative Scenario 3: Access Full financing for Paediatric amoxicillin oral solution*



Outcomes of Scenario 4: Watch – Pooled procurement with stockpile and minimal catalytic financing

To address shortages and affordability issues.

Antibiotic archetype: Medium-volume products, possibly off-patent.

Exemplar drug:

a. ceftriaxone; 1g; injection parenteral (Watch)

Tools	
Mechanism	Pooled procurement
	Regional revolving stockpile
Supplier-facing models	Unit costing
Country financing	Catalytic Subsidy

Outputs for countries within the pooling mechanism

SECURE Costs for Mechanism

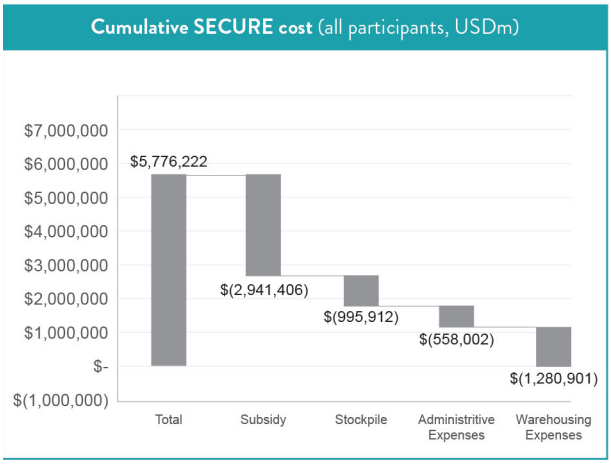
For a single Watch drug (based on ceftriaxone; 1g; injection parenteral), this mechanism has a higher cost than scenario 3 due to drug prices, as well as warehousing and stockpile costs with a need for USD 5.7 million over 5 years. Costs include subsidies (USD 2.94 million), stockpile costs (USD 0.998 million), warehousing expenses (USD 1.28 million), and administrative costs (USD 0.56 million).

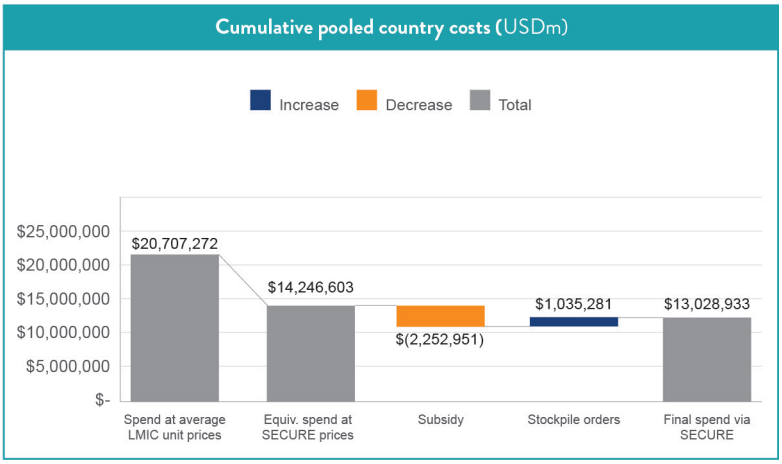
Country costs and savings

Country spend would decrease by 37% from the discounts of pooled procurement and through improved vendor management (during a 5-year period), a total saving of USD 7.7 million over 5 years for the 100 million pool. Incremental savings result from pooling (USD 4.14 million), from long-term contracting (USD 2.32 million) and from subsidies (USD 2.25 million) but also an incremental cost from accessing the stockpile (USD 1.03 million) have been factored in.

Figure 10 *Outputs for Scenario 4: Watch – Pooled procurement with stockpile and minimal catalytic financing*

Key scenario outcomes | **Antibiotic:** Medium price, medium volume, registered | ceftriaxone (parenteral)





Alternative options to reduce risks to SECURE:

Alternative options include shifting the administrative costs to the countries which would reduce the costs to SECURE to a nominal amount, while still enabling substantial cost savings for countries (savings reduced from 37% to 35%). The strong volume-based discounts and vendor management savings more than offset the addition of a small fee to cover procurement services.

Outputs for countries outside of the pooling mechanism

As an extension of this scenario, once the pooled procurement mechanism is established additional countries would be able to access the stockpile only without participating in the pool or receiving the subsidy

- SECURE costs: SECURE has little additional costs as the country only accesses the stockpile and does not participate in the pooled procurement mechanism. Over 5 years, it will reduce the cost of the mechanisms for SECURE by USD 10,700 for every additional country accessing only the stockpile.
- Country costs and savings: Each country could independently access the stockpile in case of shortages for an incremental cost (above their current baseline cost for the product) of 7.5%.

Benefits

This scenario supports affordability through pooling, quality assurance by limiting supply to quality-assured vendors, and provision of quality control procedures via the pooling mechanism, as well as supplier diversity. Additionally, the stockpile provides supply security in case of forecasting errors, surges or other shortages. Additional flexibility is added, whereby countries not participating in the pooled procurement mechanism can leverage the framework agreement and buy directly from the suppliers.

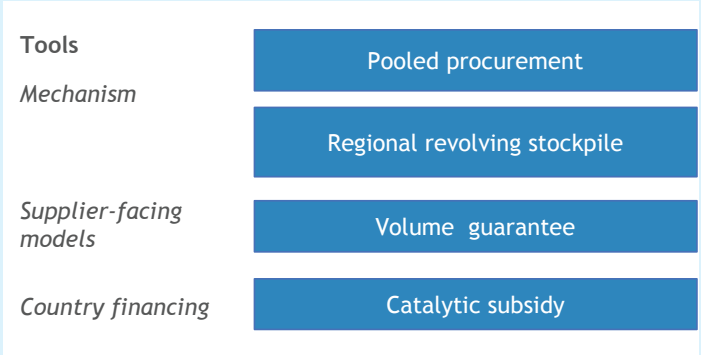
Outcomes of Scenario 5: Reserve – Pooled procurement, stockpile, volume guarantee and catalytic financing

To address key access issues related to on-patent, often newer, low volume products usually in the Reserve category with pooled procurement, supplier guarantee and country subsidies.

Antibiotic archetype: High priced, low-volume product, not registered in country.

Exemplar drug:

a. ceftazadime-avibactam 2.5 grams parenteral – Reserve



Outputs for countries within the pooling mechanism

SECURE Costs for Mechanism

For a single product (modelled based on ceftazidime/avibactam IV), savings for a single country are estimated at USD 1.063 million over 5 years. It is due to minimal volumes needed with the potential to receive the drug at a more than 80% reduction based on the estimate of an average LMIC price. Total savings for the entire pool of countries would potentially amount to USD 8.86 million.

It would cost USD 3.64 million (USD 4.552 million) to establish the mechanisms for the pool of countries, comprising procurement services, catalytic subsidy as well as a supplier guarantee. The majority of this cost is from the subsidy to countries (USD 2.8 million), warehousing costs (USD 0.251 million), administrative expenses (USD 0.109 million) and stockpile costs (USD 0.447 million).

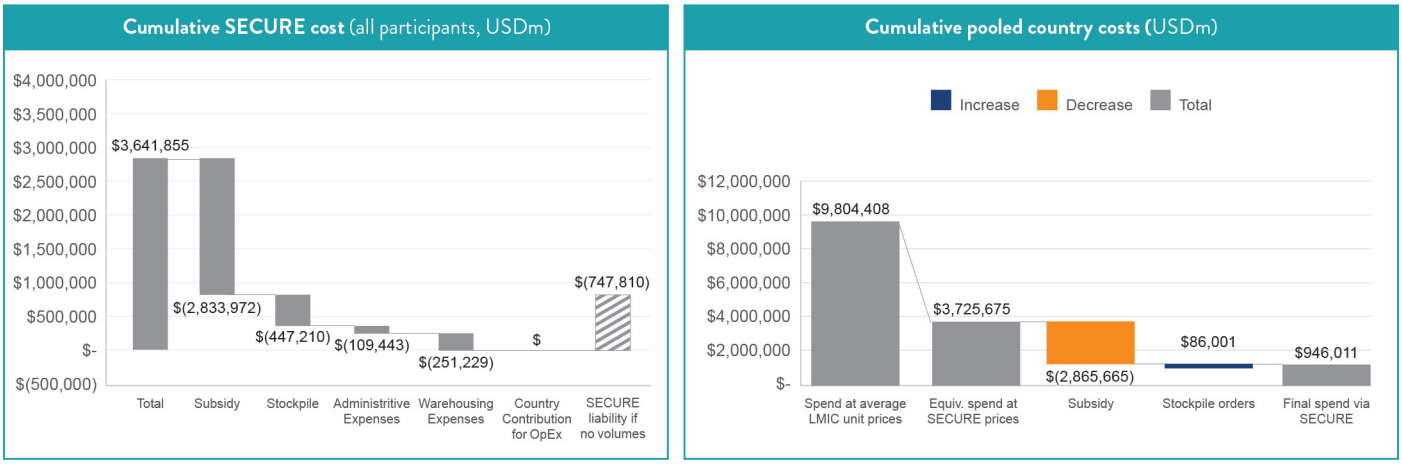
SECURE would need to provide an additional supplier guarantee liability of USD 0.748 million, if purchases by countries don't meet the guaranteed amount. It is modelled that the entire pool will purchase up to the expected volume guarantee by year 5.

Country costs and savings

Countries purchasing through the pooling mechanism would reduce their spend by more than 80% based on the reduction in price, pooling impact and subsidy[16]. Their spend over the 5-year period, will reduce from USD 9.8 million to USD 0.946 million. Most of the savings result from pooling (USD 5.88 million) followed by the subsidy scheme (USD 2.86 million) with a small reduction from the volume gaurantee (USD 0.196 million). There is an additional cost for orders via the stockpile (USD 0.086 million).

Figure 11 - *Outputs of Scenario 5: Reserve – Pooled procurement, stockpile, volume guarantee and catalytic financing*

Key scenario outcomes | **Antibiotic:** High price, low volume, not registered | ceftazadime-avibactam



16 SECURE subsidises 95% of the cost for drugs in year 1 and year 2; 79% in year 3, declining thereafter at a rate of 5% per annum.

Alternative scenarios to reduce costs to SECURE

Should the stockpile be removed from this scenario for countries this would reduce SECURE costs by 12% while only marginally improving countries' costs (USD 0.086 million) over the 5 years.

Should the subsidy be reduced to 20% each year, then the cumulative costs for SECURE would be reduced by 63%, whereas the country pool will face a three times higher costs (USD 3.3 million versus USD 0.946 million). over the 5-year period) However, it is still a 66 % reduction on the average LMIC prices.

These alternative scenarios will not impact the incentives for the manufacturers to enter the market, however, the removal of the stockpile is likely to reduce supply security due to the erratic nature of demand for these low volume antibiotics and sudden surges related to outbreaks.

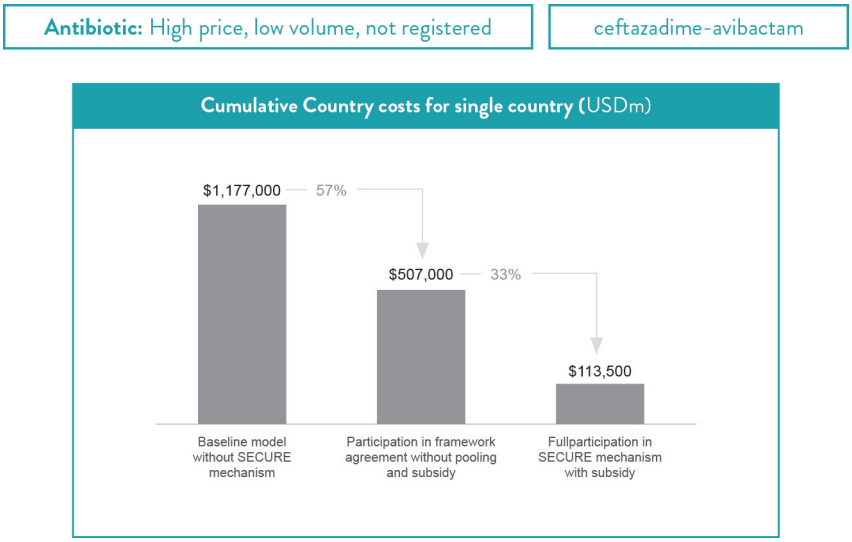
Outputs for countries outside of the pooling mechanism

Once the pooling mechanism is established, new countries may, under specific circumstances[17], be able to access pooled pricing and remain outside of the pooling mechanism. They can leverage the framework agreement and buy directly from the suppliers with the SECURE reduced rate (with additional 5% fee on the post-pooling price). The country would still be required to submit demand forecasts to manufacturers.

SECURE Costs for Mechanism: SECURE has no additional costs or financial liability as the purchase orders go directly from country to manufacturer using the framework agreements negotiated by the PSA. However, there may be a need for technical assistance for demand monitoring/forecasting or oversight for stewardship in these countries (not factored into the costing model).

Country costs and savings: The single country has a potential price reduction of 57% from pooling alone saving USD 0.670 million (incl. 5% fee;). This reduced price is 4,5 times more than a country participating fully in the pooling mechanism would pay.

Figure 12 - *Comparison of country costs between full and partial participation options*



17 Where pooling is not an option for the country due to regulatory procurement controls or policies.

Benefits

Countries:

- Negotiated/discounted per unit price for higher cost antibiotics (pooling, subsidy and volume guarantee)
- Subsidy is substantial but not 100% requiring countries to allocate some budget and work towards self-sustaining financing
- Access to a stockpile which can smooth out uncertain demand and initial forecasting inaccuracies
- Any country may leverage SECURE framework agreement to buy at discounted rate with some additional mark up to cover adhoc nature of these purchases

Suppliers:

- Facilitated market entry and registration through SECURE mechanism
- Aggregated larger volumes through pooling
- Improved predictability and visibility of demand with pooled forecasts/ estimates
- Surety of payment from guarantee and through PSA payment terms

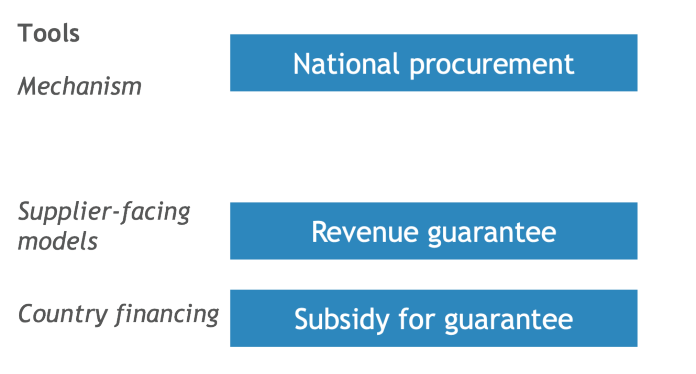
Outcomes of Scenario 6: Reserve – Single country revenue guarantee

To address key access issues related to on-patent, often newer, low volume products usually in the Reserve category for a single country with a revenue guarantee only.

Antibiotic Archetype High price, low volume.

Exemplar drug:

a. ceftazidime/avibactam parenteral - Reserve



SECURE Costs for Mechanism

As SECURE will finance 50% of the revenue guarantee on a yearly basis, the cost for mechanism for the single country is USD 1 million over the 5-year period with a guarantee liability of USD 2 million. The financial commitment increases as more countries are supported with individual revenue guarantees.

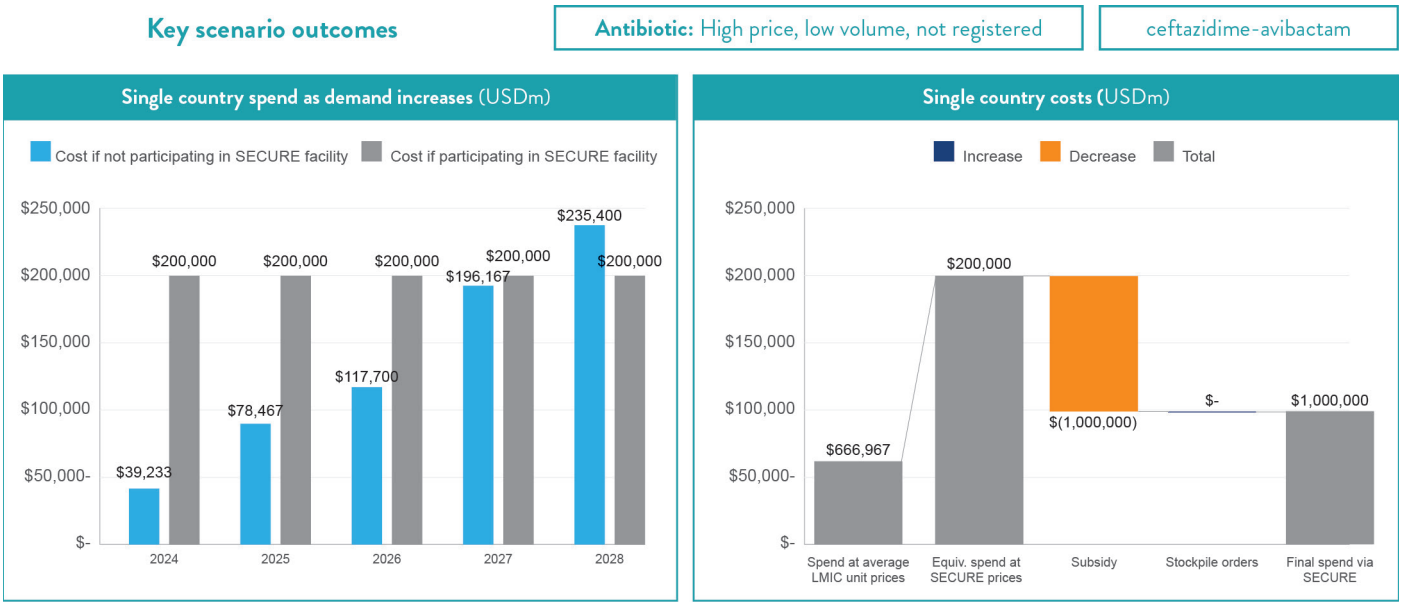
Country costs:

Country spend, over 5 years, would increase by an effective 50% due to the additional revenue guarantee meaning their baseline costs of USD 667,000 (if they purchased according to demand and the average LMIC base price) would go up to USD 1 million to secure access to this drug. The saving from the SECURE subsidy of the guarantee is offset by the cost of the country's portion of the revenue guarantee (USD 1 million) with a net additional amount of USD 333,000 having to be paid.

Benefits: Accessibility of newer (usually Reserve) drugs for LMICs through registration and the revenue guarantee.

As this model is driven by country scale up of demand towards the level of the guarantee, stringent stewardship principles will need to be implemented to ensure appropriateness of use. This model was judged to have low feasibility as countries would be unlikely to agree to a revenue guarantee given their low historical demand and need to prepay for access to be secured.

Figure 13 Scenario 6: *Reserve – Single country revenue guarantee*



Summary of Key Findings & Recommendations

Provisional findings indicate that SECURE has high potential to support access to antibiotics by implementing the following tools: pooled procurement, supplier guarantees, temporary catalytic product subsidies or financing support to countries, and stockpiles. Benefits include improved affordability for countries, incentivized market entry and predictability of demand for suppliers, surety of supply and quality-assured products available in countries.

The tools which have the highest potential included:

- Pooled procurement, strengthened forecasts and long term contracting, is effective to achieve the best reductions in price from the manufacturers
- Revolving stockpiles, which are continuously resupplied and replaced as drugs are purchased by countries. These stockpiles are linked to pooled procurement mechanisms
- Catalytic subsidy as a mechanism to improve affordability for more costly quality-assured antibiotics
- A supplier guarantee, based on either a minimum revenue or volume, that is sufficiently attractive to register and supply the product in the countries:
- In the case of the volume guarantee, volumes forecasted based on levels of appropriate use
- Should the minimum revenue needed for suppliers exceed estimated demand, i.e. more volume would need to be guaranteed than what would be required for appropriate use, a revenue guarantee would be more appropriate
- In either case of a volume or revenue guarantee, should the demand exceed the minimum volumes determined in either the volume or revenue guarantee, then the product will be paid for at a unit cost at the agreed price. This is similar to the Swedish model of revenue guarantee

The combination of tools is highly dependant on the antibiotics and their country specific access challenges.

We tested six different scenarios of which three were found to have the highest potential to improve access in an economically feasible way. Ultimately, a balanced portfolio of “Access”, “Watch” and “Reserve” antibiotics would need to be created and modelled for feasibility. This would enhance stewardship and match national treatment guidelines and country needs.

See a brief summary of the most viable scenarios in Figure 1 overleaf. It provides the key results for the package of tools applied to each antibiotic archetype using a sample antibiotic. Results are shown in terms of overall cost savings to those participating in pooling, potential product price discount, and estimated cost of implementing the contracting of the mechanism to a procurement entity over 5 years.

Figure 14 – *Scenarios showing good potential for SECURE to flexibly address country-specific needs.*

Antibiotic Archetype	Tools	Antibiotic example (single drug per archetype)	Pooled Country savings over 5 yrs[1]	% price reduction potential[2]	Costs of mechanism over 5 yrs[3]
1. Registered, low price, high volume	Pooled procurement + revolving Stockpile	"Access" antibiotic (amoxycillin oral solution)	USD 4.15 million	16%	USD 3.2 million
2. Registered, medium price, medium volume	Pooled procurement + revolving stockpile + with catalytic subsidy	"Watch" parenteral antibiotic (ceftriaxone IV) (subsidy applied at 25% and declining thereafter)	USD 7.68 million	37%	USD 5.78 million
3. Non-registered, high price, low volume	Pooled procurement + revolving stockpile + supplier guarantee + catalytic subsidy	"Reserve" antibiotic (ceftazidime/avibactam IV) (subsidy applied at 95% and declining thereafter)	USD 8.86 million	>80%	USD 3.64 million + USD *0.748* million[4]

1. Savings calculated at average LMIC price for a small country (e.g.,Tunisia) for an individual antibiotic and summed up for the entire 100 million population pool
2. Discount based on average LMIC price for antibiotic
3. Mechanism includes contracting with an existing Procurement Entity - service fees, stockpile, warehousing and wastage costs
4. SECURE volume guarantee liability should one be included for the countries in the pool

Please note: These numbers are indicative only with large uncertainty margins and are meant to illustrate the potential benefits and costs of different tools.

A. Scenario to address access issues for high volume, off-patent antibiotics characterized by low margins. These antibiotics were often in the "Access" category such as paediatric formulations – Archetype 1

The package included aims to create a predictable, more efficient and sustainable market for suppliers, while also providing insurance against shortages. This could also improve the affordability of quality-assured products.

The relatively lower volumes of these pediatric access products reduced the revolving stockpile, administration and warehousing costs when compared with other types of access products and still provided for a 16% price reduction. The stockpile in addition, allows a buffer stock to protect against shortages.

B. Scenario to address access issues for antibiotics that are of medium volume, on or off-patent. These antibiotics were often classified under the "Watch"– Archetype 2

Similar to the previous scenario, the package created a predictable, more efficient and sustainable market for suppliers, while also providing insurance against shortages and availability of higher quality products. In addition, the SECURE catalytic subsidy improved affordability with an estimated 37% price reduction. This mechanism has the highest cost due to the subsidy, expensive warehousing and stockpile costs with a need for USD 5.78 million over 5 years for a pool of 100 million population.

C. Scenario to address key access issues related to on-patent, recently introduced, low volume highly priced products. These antibiotics are typically Reserve Archetype 3

The package to improve access to Reserve antibiotics focuses on creating a market for the supplier that is more coordinated, predictable, and consolidated (with relatively larger volumes) to improve affordability and expand availability. Interventions to reduce introduction barriers were also included for these products which often are more expensive or more difficult to introduce.

Key stakeholders have confirmed that this model would improve market attractiveness for manufacturers and support access and affordability for these antibiotics into geographies previously not considered attractive. The risk with increased accessibility is inappropriate use and therefore stewardship interventions are a critical component in this scenario. Participating parties can help support stewardship by implementing a new product introduction strategy for phased and monitored introduction, appropriate use and training of prescribers. SECURE should also work with countries to ensure that demand does not shift use in favour of Reserve antibiotics as they become more available, and their affordability improves. Therefore a balanced portfolio of "Access", "Watch" and "Reserve" antibiotics is needed.

D. Models found to be less feasible

Several other procurement and economic packages were tested which were found to be less feasible. This included using a stand-alone rotating stockpile for emergency supply without pooling to address global shortages of high-volume "Access antibiotics". The costs to run such a stockpile were estimated at USD 15.3 million (modelled on amoxicillin capsules). The countries are in effect also paying an additional 10% towards the costs of holding such a rotating stockpile. This is not likely to be economically feasible or effective, as the choice of stockpile size will depend on the severity of expected shortages and the ability to predict which antibiotics and which countries may be prone to shortages, so that the stockpile can be placed in the correct region.

Full financing mechanism for Access antibiotics, in which SECURE subsidies 100% of the product costs, requires extensive and sustained funding (USD 32.3 million for a single drug for 5 years for a pool of 100 million population). This would improve access, but at the same time reinforce dependency on external financing for long term provision of antibiotics. As such, it would only be considered for very special cases.

While full financing is less feasible pooled procurement and stockpiling mechanism are still a viable option alongside other supportive interventions by SECURE to address global shortages of high-volume Access antibiotics.

For example, countries can optimize their Access antibiotic portfolios and focus procurement to support market consolidation. The increased volume demand for a given antibiotic may allow countries to also support good procurement practices like split tenders, thus reducing risks of shortages for a single supplier. SECURE can support countries with improved market intelligence and more reliable forecasting models. Finally SECURE can advocate for national regulatory authorities to address shortages by supporting supplier mapping, requiring suppliers to report anticipated shortages and disseminating information on forecasted demand.

It is not feasible for LMICs to agree to upfront supplier guarantees for Reserve antibiotics such as Scenario 5 with a single country revenue guarantee even with 50% SECURE subsidy, given their low historical demand and their limited public health funds. Such supplier guarantee models may be tried as innovative pilots with interested countries once the SECURE mechanism is functional with proven benefits.

Limitations of the modelling

The model itself has limitations including the following:

- The model was based on available data for drug prices and consumptions levels. The available data may be incomplete and not suitable across multiple different country types. Therefore the cost savings, price reductions and expenses of the mechanisms have large uncertainty margins and are meant to illustrate the potential benefits and costs of different tools. These assumptions will need to be discussed with countries, potential manufacturers, distributors, and procurement entities to help refine the economic model
- Each Archetype had only one exemplar drug selected for modelling purposes. Ideally a portfolio of multiple "Access", "Watch" and "Reserve" antibiotics would need to be created and modelled so that it is feasible and suitable for the country's needs
- Countries in the 100 million pool were all of the same economic income level. However having a mixture of various income levels and sizes of countries in a pool will allow for cross subsidisation using tiered pricing. This will allow for price reductions for all, whilst supporting the best economic solution for the lowest income countries
- The economic and procurement tools were modelled as a package of interventions. It might be feasible to exclude a procurement mechanism and rather provide stand-alone supplier guarantees or alternatively catalytic financing for more unaffordable products.

Therefore the results are indicative only with large uncertainty margins and are meant to illustrate the potential benefits and costs of different tools.

Risks for mitigation

The models contain risks including:

Risk for the Set up of the mechanism

Risks relate to the set-up of the procurement entity and mechanism. Countries may be uncertain about the potential benefits, resulting in lack of national political will to participate. To ensure sustainability, country subsidies will need to be continued over a longer period requiring additional donor funding. Suppliers might not be incentivized to agree on price reductions, despite the benefits of market consolidation, improved predictability and supplier guarantees. If there is not sufficient take up by countries or it takes too long to set up, then the economies of scale impacting on pricing may be undermined. The contracted procurement agencies will form long-term relationships with suppliers and implement further interventions that may incentivize supplier engagement. The procurement entity will also work with countries to support their forecasting using an antibiotic forecasting tool developed by SECURE.

Operating risks

Operating risks include inaccurate forecasts and delayed payments or payment defaults by countries. There is also a risk that countries don't buy the products for which supplier guarantees are provided, thereby requiring the guarantor to step in and pay. A suitable financial backer and donor to support the establishment of the mechanism will need to be secured. To ensure sustainable supply it is crucial to implement tendering that looks at criteria beyond price.

Distributors could export discounted-priced products to neighboring countries and sell at higher prices. This could lead to in-country demand fluctuations and stock-outs.

Countries might not adhere to forecasting and stewardship monitoring mechanisms, undermining the ability to preserve the effectiveness of these antibiotics.

Risk related to Stand-alone Rotating Stockpiles

- It will be difficult to determine the right size of the stand-alone rotating stockpile. This would depend on accurately predicting which antibiotics may be at risk, as well as the severity, geographic impact, and duration of shortages. It could also be difficult to prioritize countries for distribution of stock in case there are significant or long term stockouts.
- Another challenge is where to strategically place the stockpile in a region so that it can be transported to countries efficiently and at the lowest cost. Additionally, should a shortage be severe or long-term, the stockpile may not be sufficient to cover all the needs of all countries' for the duration of the shortage. Finally, if the stockpile is not needed then the entire stock will be wasted and reflect as a financial loss.

Risk related to Reserve Antibiotic archetypes

Preserving the power of antibiotics, especially the "Reserve" class is extremely important for SECURE. Providing access to "Reserve" antibiotics needs to be coupled with the availability of "Watch" and "Access" drugs which treat the same infection or disease syndrome. If countries don't consistently monitor and report interventions this may complicate management of stewardship, and lead to reluctance by suppliers to expand the mechanism.

Risks of purchasing from the long-term agreements without being part of the pooling mechanism (flexible option)

Selected manufacturers may not agree to allow countries outside of the pooling mechanisms to directly procure at the discounted prices. They may not have additional production capacity should orders from these countries exceed their forecasts. The mechanism may break down if countries are allowed to access the same prices enjoyed by countries in the pool. This may also disencentivize other countries from joining. SECURE will work directly with countries to understand their needs and identify suitable ways to facilitate these mechanisms.

Manufacturing side risks

Manufacturers may still be reluctant to build additional manufacturing capacity if needed, due to lack of long-term agreements or insufficient volumes in the pool.

If an import waiver is not granted by the country, the manufacturer may not be incentivised to file their product.

In order to mitigate risks, SECURE will work directly with countries to understand their needs and identify suitable ways to facilitate these mechanisms. Participating procurement agencies will form long-term relationships with suppliers and implement further interventions that may incentivize supplier engagement. The procurement entity will also work with countries to support their forecasting using an antibiotic forecasting tool developed by SECURE.

Key takeaways to mitigate risk and next steps for SECURE

SECURE can play a key role in improving access to appropriate essential antibiotics. Three packages of interventions tailored to key access issues of common drug archetypes were deemed feasible and provide a very promising financial case to begin SECURE's implementation. Savings were shown for countries as compared to their average cost baselines, while the cost to create the mechanism with an existing procurement entity is deemed to be reasonable and sustainable compared to other scenarios tested. Discussions on specific access challenges and possible economic solutions with countries, potential manufacturers, distributors, and procurement entities will help to further refine the economic model.

It is important to note that SECURE will work directly with, as well as through partnerships with organizations and countries to encourage their solidarity. Stakeholders supported use of existing international or regional pooled procurement entities and the selection of the right entity or entities will be crucial to SECURE's success.

It is envisioned that, in collaboration with countries, a small portfolio of "Access", "Watch", and "Reserve" antibiotics will be identified by early 2024 to test the SECURE model. Products will be selected which have strong public health importance and persistent access challenges, widely applicable to many countries. Impacts and costs will be modelled; this more concrete and granular data will facilitate discussions with potential partners in the implementation phase, including participating countries.

In the next phase of SECURE, regional and country discussions will aim to tailor and combine the economic and procurement tools with the broader SECURE interventions which addresses individual product and country needs.

SECURE can support countries with additional interventions to optimize their antibiotic portfolios, improve market intelligence and more reliable forecasting models and can advocate for national regulatory authorities to address shortages. Determining the most practical stewardship levers which is included within the SECURE interventions, will go hand in hand with the portfolio decisions and require a country-specific lens.

ANNEXURE A: Sources and key stakeholders involved in project

Initial Sources | Conducted 17 interviews & consulted various secondary sources

Interviews
17 internal, external, and GARDP-facilitated interviews

Name(s)	Organization	Organization type
Greg Frank & Paul Schaper	Merck	Branded manufacturers
James Anderson	IFPMA	Branded manufacturers
Agam Goel & Mitali Thakur	BCG (India healthcare proc.)	Internal
Emily Serazin	BCG (GAVI lessons learned)	Internal
Guervan Adnet	BCG (AMR)	Internal
x2 Anthony McDonnell	CGDev	International stakeholders
Rene Berger	Management Sciences for Health	International stakeholders
Brenda Waring	Global Drug Facility (Stop TB)	International stakeholders
Cynthia Kamtengeni, Sebastian J. M.	UNICEF	International stakeholders
Carlos Correa	South Centre	Country-level experts
Sarang Deo	India (ISB)	Country-level experts
Daniel Teferi *(externally arranged)*	Ethiopian MoH, USAID (Ethiopia)	Country-level experts
Dwi Pusupari *(externally arranged)*	Indonesian Public Health Ministry	Country-level experts
Francis Maingi *(externally arranged)*	SAI Pharma, USAID (Kenya)	Country-level experts
Nasir Idrees *(externally arranged)*	UNDP/UNPF/UNICEF (Pakistan)	Country-level experts
Vu Quoc Dat *(externally arranged)*	Hanoi Medical University	Country-level experts

Secondary research
Non-exhaustive list

Policy briefs & other grey literature
- *Antimicrobial Resistance Research Programme Study #1* (Access to Medicine 2022)
- *Access Barriers to Antibiotics* (CDDEP 2019)
- *Antimicrobial Resistance: Multi-Partner Trust Fund Report* (WHO 2021)
- *Future Global Governance for Antimicrobial Resistance* (UNSG 2018)
- *Grand Bargain for Antimicrobial Proc.* (CGD 2022)
- *Improving access to essential antibiotics* (Access to Medicine 2021)
- *Leveraging Purchasing Systems to Ensure Access, Stewardship, and Innovation* (CGD 2022)
- Policies & interventions to improve access to next-gen. antimicr. in LMICs: India case study (CGD, ISB 2023)
- The How of Pooled Procurement (MSH 2022)
- The Why of Pooled Procurement (MSH 2022)

Academic literature
- *Antibiotics* (Gautham et al. 2022)
- *Bulletin of the World Health Organization* (Knowles et al. 2020)
- *Globalization & Health* (Brogan & Mossialos 2013, Parmaksiz et al. 2022)
- *Regulatory Rapporteur* (Alquier 2021)
- *The Lancet Global Health* (Do et al. 2021, Sulis & Gandra 2021)

Model assumptions | 12 additional interviews conducted to develop and confirm hypotheses

Name	Organization	Organization type
Greg Frank & Paul Schaper *(follow-up)*	Merck	Branded manufacturers
Wesley Kreft	I+Solutions	PSA
Sowedi Muyingo	Medical Access Uganda Limited	PSA
Guervan Adnet *(follow up)*	BCG (AMR, GF)	Internal
Abhishek Gopalka	BCG	Expert India
Tolu Oyekan	BCG	Expert Africa HS
Peter Barton	Bill & Melinda Gates Foundation	International stakeholders
Anthony McDonnell *(follow-up)*	CGDev	International stakeholders
Olatunde Sanni	Procurement & Supply Mgment (Nigeria)	Country-level expert
Christian Guyader	BCG	International stakeholders
Benjamin Loevinsohn	Gavi	International stakeholders
Greg Fischer	BCG	Expert innovative finance

Leveraged to test models and confirm assumptions

ANNEXURE B: – Introduction to SECURE

SECURE is an innovative initiative being developed by World Health Organization (WHO) and the Global Antibiotic Research and Development Partnership (GARDP) to improve access to both existing and new antibiotics.

The antibiotic access challenge

Access to essential antibiotics is a vital component of the global response to antimicrobial resistance (AMR) and overall pandemic preparedness. Existing antibiotics (which are often generic) are increasingly subject to supply interruptions in low-, middle- and high-income countries (LMICs) alike, or are simply not available. As a result, the best tools for combating infections fail to reach those in greatest need, and the subsequent use of alternative antibiotics contributes to the development and spread of resistance. At the same time, newer products especially Reserve[18] antibiotics, have limited access because of low and erratic volumes and high prices. Demand is therefore limited and as a result, products are often not registered or supplied in many countries, particularly in LMICs.

SECURE will increase access to a **portfolio of quality-assured antibiotics in a sustainable, equitable and appropriate way.** It will improve appropriate access **to both existing and new antibiotics.** SECURE's antibiotic portfolio will be adapted to meet national public health and clinical needs.

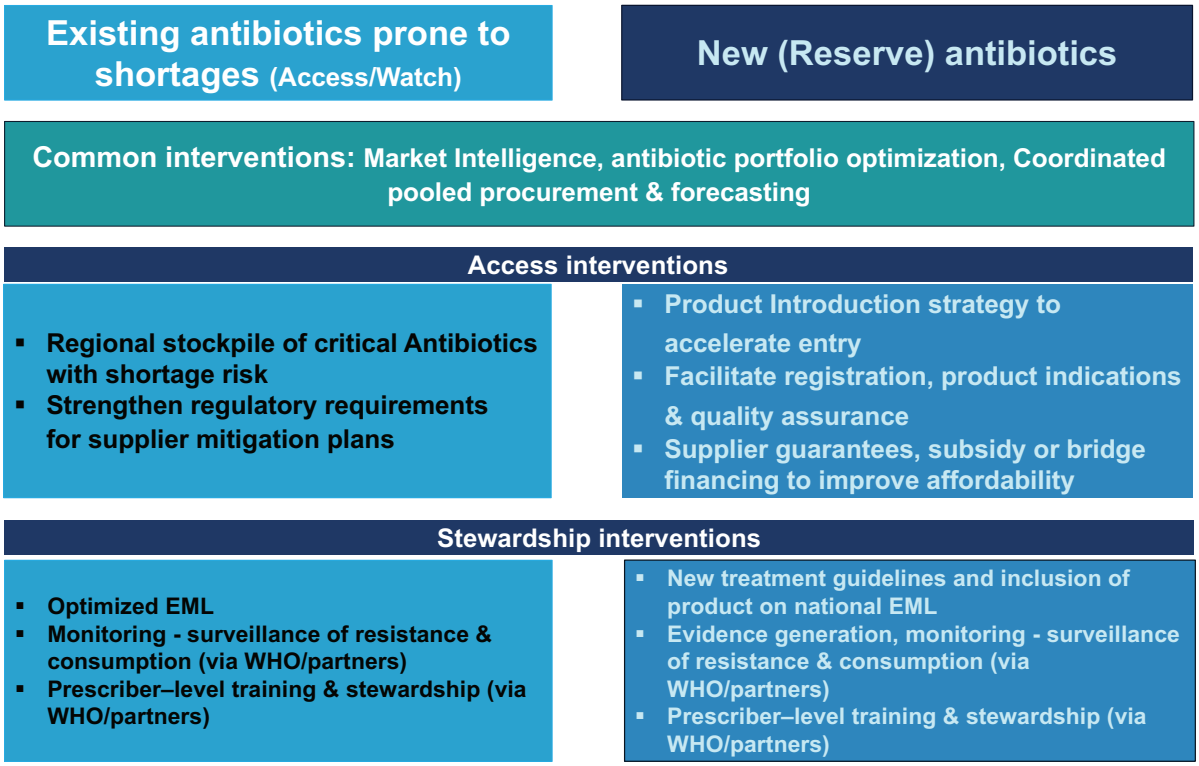
SECURE's Value Proposition - What will SECURE do?

- SECURE will increase demand predictability and attractiveness for suppliers by aggregating demand across countries:
    - SECURE is creating an **antibiotic forecasting model** to support pooling, stockpiling and contracting with suppliers, using a prioritized portfolio of antibiotics
    - SECURE is embarking on work with existing procurement mechanisms to establish **pooled or coordinated procurement mechanisms**
- SECURE will implement measures to address recurrent antibiotic shortages, including Identifying the need for **stockpiles** of selected antibiotics and working to establish these within existing systems.
- SECURE will establish mechanisms to collect and collate **antibiotic and supplier market intelligence** to improve decision-making on procurement, warn of shortages and identify priorities for expanded manufacturing, including domestic manufacturing.
- SECURE has evaluated how **economic tools** can be used to incentivize suppliers to enter country markets and support country purchasing through catalytic financing methods. SECURE aims to apply and test these tools as part of an overall proof-of-concept of the SECURE model.
- Working through partners at country and regional level, SECURE will support:
    - the simplification of antibiotic portfolios through **prioritization, optimization or harmonization at a country/regional level**, which will support clinical best practice and improve the efficiency of forecasting and procurement and supply.
    - Gathering **real-world evidence on the local use of antibiotics** and monitoring both consumption and resistance, to inform updated treatment guidelines as well as forecasting and procurement, and evaluate the impact of SECURE interventions.

18 Based on the World Health Organization AWaRe classification of antibiotics – Access, Watch and Reserve. https://www.who.int/publications/i/item/2021-aware-classification

Recognizing that the access challenges of existing and new antibiotics are different, SECURE has defined a set of tailored interventions that target each of these antibiotic types (Figure 1)

Figure 1 – *SECURE interventions tailored to antibiotic types*



Stewardship is at the core of SECURE - The introduction of new (often Reserve) antibiotics, needs to go hand in hand with monitoring their appropriate use, as well as governance structures and polices to protect the longevity of antibiotics. SECURE will work with countries to support optimization of their broader antibiotic portfolio and by developing product introduction pathways. This will be supported by broader operational guidance being developed by WHO on the introduction and preservation of new Reserve antibiotics. Stewardship activities could also include working with country partners to create guidelines and provide training for prescribers, if required.

SECURE will also work with relevant partners to support stewardship as part of product registration and regulatory interventions, for example through the inclusion of specific drug registration product indications; marketing and labelling requirements; data reporting requirements; and quality assurance of products.

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Expanding Sustainable Access to Antibiotics

February 2024