

# How portfolio-based product development can accelerate progress in global health

Lessons learned from PATH's G6PD Diagnostic Initiative





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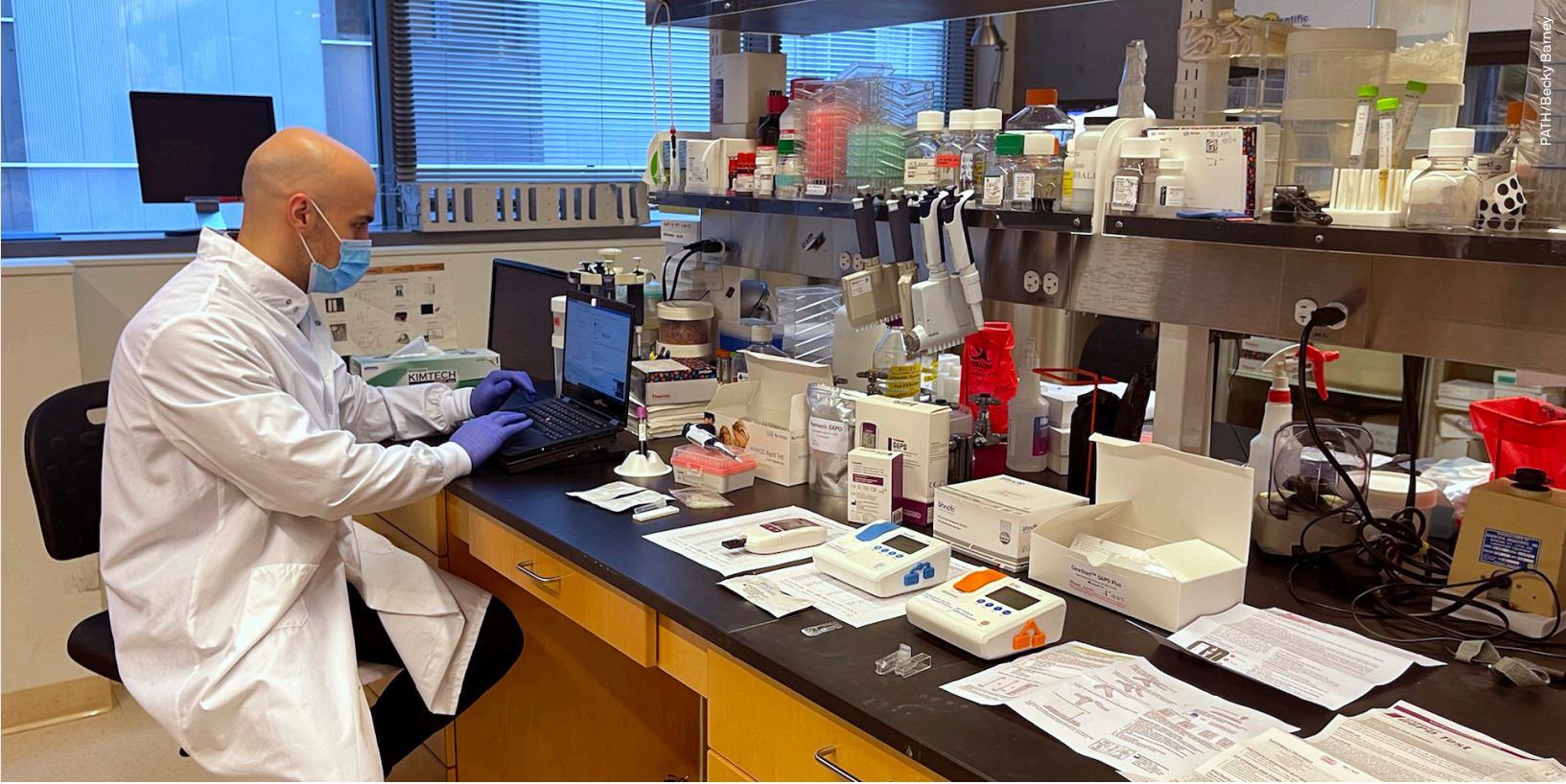
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Contents

A product development partnership	1
Establishing a portfolio strategy	2
A new G6PD test: the missing link for curing one type of malaria	4
Developing the TPPs	6
Forecasting market size, demand, and risks	7
Assembling the portfolio	8
PATH’s R&D support	10
Progress and setbacks	11
A more streamlined portfolio	12
PDPs: looking ahead	14
Resources	15
Resource A: Lessons learned	15
Resource B: Probability of Success tool	18
Resource C: Governance structure	22
References	25

On the cover: Testing the usability of a prototype G6PD point-of-care test with health workers in Laos.

Photo: PATH/Spike Nowak



A lab worker reviews results from the evaluation of several G6PD test prototypes.

A product development partnership

**BILLIONS OF PEOPLE AROUND THE WORLD SUFFER** from infectious diseases and other poverty-related health problems for which low-cost, easily accessible medical products—such as vaccines, diagnostics, and treatments—are not available. Private-sector companies have limited incentive to enter these markets because such products can be expensive and time-consuming to develop, the chances of technical failure during development are high, and the potential for profit may be minimal in low- and middle-income settings.

Over the past two decades, a critical tool for innovation in global health has emerged to address this gap: the **product development partnership (PDP)**, which brings together public, private, academic, and philanthropic expertise and funding to develop and deliver global health products that would otherwise have little or no chance of coming to market.<sup>1</sup>

Many of these PDPs take a **portfolio-based approach**, spreading investments among multiple companies

to increase the probability that at least one viable product will emerge to meet the need.<sup>2</sup>

The benefits of PDPs, including the portfolio-based approach, have been widely noted but not often documented. This paper examines one effort, PATH’s G6PD Diagnostic Initiative, to highlight key factors that can lead to challenges and contribute to success. Although each PDP is unique, and PDPs can vary greatly in scale, scope, and the number and configuration of partners, many of the lessons from this initiative are broadly applicable to other global health efforts and may be helpful to funders, product developers, policymakers, and researchers as they consider engaging in PDPs. Notably, the US government used a portfolio-based PDP approach to fund development of vaccines against the virus that causes COVID-19, but that scenario was an extreme outlier in terms of the scale of potential demand—and profit—for products resulting from PDPs.

# Establishing a portfolio strategy

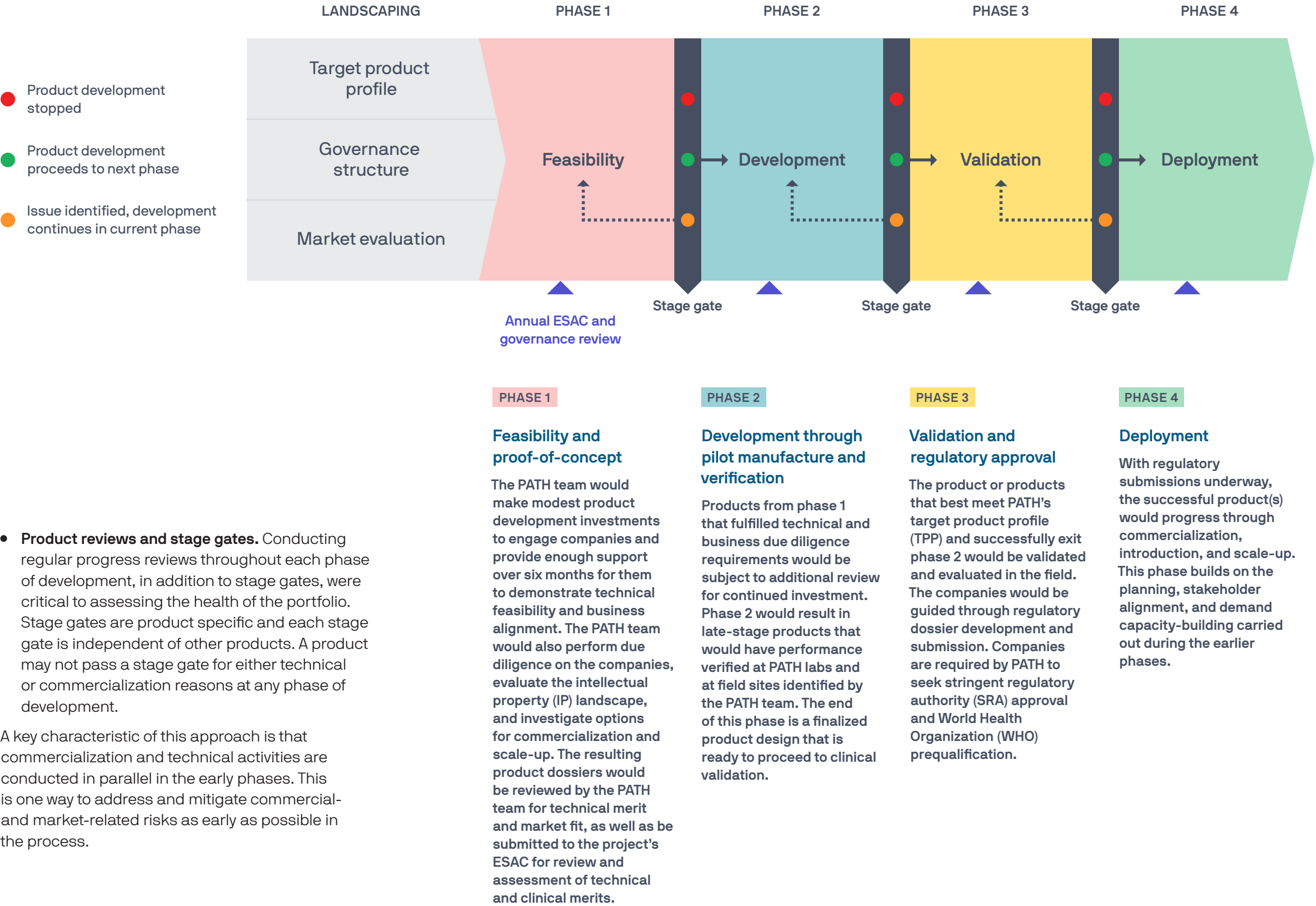
For some PDPs, a portfolio-based approach may be the most appropriate strategy, given the significant commercialization and technical risks associated with developing and deploying health tools. Some of these risks may be universal, but risks can also be associated with a particular developer or organization or the type of global health tool in question. The portfolio itself may be composed of products from a variety of the product development phases and from different companies as a risk mitigation for some of those products not advancing.

PATH implemented several important tools to ensure sound decision-making:

- **A governance structure.** Establishing a governance process and structure before making any investments (see “Resources” for details) ensures balance and transparency for all parties involved. PATH’s structure included an independent advisory board—called the External Scientific Advisory Committee (ESAC)—to review the entire portfolio of products annually and set expectations for decision-making processes.
- **A phased approach.** Using a phased approach to product investments and stage gates, a series of decision points to determine whether a product warrants advancement to the next phase, as shown in Figure 1, provided a process for removing technologies at earlier stages. This allowed PATH to pivot funding to alternative technologies and kept multiple products in play, resulting in a higher likelihood of success (“Resource B”).

THE TECHNICAL FEASIBILITY and quality of a product is important to establish during product development, but without a strong commercialization plan that allows the product to reach the markets where it is most needed, the investment may be lost.

FIGURE 1. Phased approach to product investments.







Examples of several types of G6PD test included in the product development partnership.

## A new G6PD test: the missing link for curing one type of malaria

**MALARIA IS A PARASITIC DISEASE THAT AFFECTS** more than 200 million people each year and leads to more than 400,000 deaths annually.<sup>3</sup> Of the five parasite species that cause malaria in humans, *Plasmodium (P.) falciparum* is the most prevalent and deadly and causes nearly all malaria cases in Africa. A different species, *P. vivax*, is most common in South and Southeast Asia and South America. As countries approach malaria elimination, the relative burden of *P. vivax* increases and often surpasses that of *P. falciparum*. Unlike *P. falciparum*, *P. vivax* produces a dormant liver-stage parasite that is killed only by a certain class of drugs, called 8-aminoquinolines. When safely administered alongside standard antimalarial drugs, 8-aminoquinolines support complete elimination of *P. vivax* from the body, in what is known as radical cure. These drugs can be life-

**A quick, highly sensitive, easy-to-use, low-cost G6PD test was needed to support safe administration of tafenoquine and primaquine.**

threatening to people with a deficiency of the enzyme glucose-6-phosphate dehydrogenase (G6PD), which occurs in 400 million people worldwide and is especially common in malaria-endemic regions.

One 8-aminoquinoline, the drug primaquine, which requires a one- or two-week course, has been used since the 1950s to treat *P. vivax*. It is given without a

requirement for G6PD testing before use because the drug was adopted in a different regulatory climate. In 2015, WHO updated its malaria treatment guidelines to recommend G6PD testing before treatment with any 8-aminoquinoline. Beginning in 2008, through a partnership with the Medicines for Malaria Venture, GlaxoSmithKline (GSK) began developing a new drug, tafenoquine, that could be administered in a single dose. Tafenoquine would require a quantitative G6PD test before being administered. No point-of-care tests, either quantitative or qualitative, were yet available that met the criteria for supporting safe use of tafenoquine or primaquine. Existing tests, of which 30 were commercially available, either required advanced laboratory facilities and skilled personnel or were unlikely to perform accurately enough to meet the clinical need.

**A quick, highly sensitive, easy-to-use, low-cost G6PD test was needed to support safe administration of tafenoquine and primaquine.**

PATH began the G6PD Diagnostic Initiative in 2011, with funding from the Bill & Melinda Gates Foundation for a landscape evaluation to identify existing G6PD tests and develop a TPP for a point-of-care test to support malaria treatment. In 2013, coinciding with GSK's proceeding to phase 3 clinical trials with tafenoquine, PATH received additional funding from



**G6PD DEFICIENCY manifests differently in males and females: males can be deficient or normal, while females can be G6PD deficient, intermediate, or normal. Tafenoquine is the first drug to explicitly call for differentiating females with intermediate activity from those with normal activity.**



**POINT-OF-CARE TESTS are necessary because most malaria patients live far from medical centers and are treated by community health workers or at small medical outposts that lack advanced medical facilities.**

the Gates Foundation and the UK government's Department for International Development (now known as the Foreign, Commonwealth & Development Office) to begin investing in a portfolio of G6PD diagnostic test candidates, with the goal of ensuring the availability of at least one test that could be used at the point of care for malaria treatment.

The PATH team's early market landscaping had identified clear challenges to ensuring the availability of a high-quality point-of-care test for G6PD deficiency, including small market size, low product price, technical difficulty of product development, and minimal regulation of products already in the market. These factors informed the donors' decision to fund a portfolio-based approach. PATH and GSK came together to initiate the formation of the G6PD PDP.

By 2018, the project had led to one commercial product, with several more in development. In 2021, the first commercial product had received SRA approval and was being introduced in malaria treatment settings in countries such as Cambodia and Laos. Several other countries began conducting feasibility studies to enable introduction of radical cure tools.

The following sections describe how the G6PD PDP progressed. It also notes lessons learned during each phase. The lessons learned are compiled at the end of the document, organized by category, for easy reference.

Developing the TPPs

The first step in setting up the portfolio was to identify the desired product characteristics and the gaps in currently available G6PD tests, given that this information was not readily available. This culminated in the development of a TPP. TPPs are important tools for PDPs because they help facilitate consensus and align expectations among donors, nongovernmental organizations, government ministries, and manufacturers on what is truly needed. TPPs are particularly helpful for manufacturers, who often do not have a clear idea of the global health need and the product characteristics that help build demand. The PATH team initially developed one TPP for a quantitative G6PD test to support tafenoquine use but realized that a second TPP was needed for a qualitative test that could be used with primaquine.

The TPP for the quantitative G6PD test, which was

refined over the course of the project, called for a low-cost portable device that a community health worker could use to quantitatively measure red blood cell G6PD activity in finger-prick samples. The minimum specification called for results produced in less than ten minutes, while the optimistic specification called for results in less than five.

The TPP for the qualitative blood test called for an instrument-free test that would differentiate normal from deficient G6PD activity levels. This test could be used with primaquine, and although it would not directly support tafenoquine use, it would be important for malaria case management in lower-tier health settings. The market lacked a high-quality, easy-to-use version of a qualitative G6PD test. Table 1 outlines the minimum requirements of desired features for both quantitative and qualitative G6PD tests.

TABLE 1. Minimum desired features of the G6PD tests.<sup>4,5</sup>

	Quantitative test	Qualitative test	Reason for desired feature
End user	Village/community health worker	Village/community health worker	The majority of malaria cases are managed at the lowest tiers of the health system
Sample type	Finger-prick	Finger-prick	Finger-prick samples are most commonly used for malaria diagnostics
Number of steps	No more than one timed step; fewer than five total steps	No more than two timed steps	Workflow should be minimal given the intended user
Portability	Portable; hand-held analyzer okay	Highly portable, no instrument	Lack of portability would limit ability to decentralize testing
Output	Numerical result on screen	Test line visible for “normal” and invisible for “deficient”	It is important to ensure accurate, clinically relevant G6PD status determination
Time to result	≤10 minutes	≤30 minutes	Time to results should align with patient load
Operating temperature	20°C–37°C; 30%–75% noncondensing humidity	28°C–34°C; 30%–85% humidity	Quantitative tests can correct for operating temperature, but qualitative tests are optimized for a more limited temperature range
Target ex-factory price	Disposable: ≤US\$3.00; ≤\$2.50 at scale Instrumentation: reader cost of ≤\$380; ≤\$250 at scale	Less than US\$2.00 (at volumes of 10 million)	Pricing should align with that of other malaria commodities but also recognize the need to be sustainable in a small market

Forecasting market size, demand, and risks

Another key early step was to understand the demand for the G6PD diagnostic devices. One goal of a PDP is to generate interest in particular markets, and an understanding of market size and characteristics can help ensure that PDP partners are able to develop a sustainable availability of products.

The PATH team’s initial forecast model of market size and demand focused on the top 20 *P. vivax*–endemic countries and incorporated estimated *P. vivax* cases, percentage of the population at risk, percentage of the population in high- and low-risk areas, and *P. vivax* as a percentage of total malaria cases. Of those 20 countries, India, Ethiopia, Indonesia, Brazil, and Myanmar represented more than 75 percent of the estimated market potential.

One element of commercialization risk was that the cost of G6PD testing would add significantly to the cost of malaria treatment because current practice did not include any G6PD testing.

A second element of commercialization risk was the sustainability of demand for the G6PD tests. Progress in eliminating *P. vivax* malaria through treatment enabled by G6PD tests would result in lower *P. vivax* prevalence over time and thus a shrinking market for the G6PD tests. The PATH team’s forecasting determined a demand of no more than 500,000 tests per year, which would be dwarfed by the market for rapid malaria tests, which is in the tens of millions.

PATH also conducted an analysis of national regulatory approval processes to assess any potential regulatory issues that could result in delay or denial of approval for a G6PD diagnostic.

Two types of risk

Every product development project faces technical and commercialization risks.



TECHNICAL RISKS are related to the product’s performance and usability. Although they are more likely to appear early in development, they can crop up at any time and must be constantly monitored. Some key questions to ask when monitoring the product are:

- Does it do what it was designed to do when used by intended users?
- Will it work in the intended environment (temperature or humidity) or setting (power requirements and robustness)?
- Can it be distributed through existing supply chains without additional requirements?

The test for G6PD deficiency was considered a high technical risk because it measures enzyme activity, which is highly sensitive to environmental conditions like temperature.



COMMERCIALIZATION RISKS are related to the viability of the product in the long term. They tend to surface later in the project, but is important to identify commercialization risks early and work to mitigate them. Some key questions to ask when monitoring the product are:

- How does the product compare to existing products? Can it be provided and used more cost-effectively than existing products or practices?
- Is there a large enough market for the product so a commercialization partner is incentivized to supply this product beyond the terms of the PDP?
- Is it priced so that health systems can afford it and commercialization partners can make sufficient revenue to cover their costs?
- How many suppliers/products are required to ensure a healthy market?

The small market size for the G6PD product presented a significant commercialization risk for its sustainability.



# Assembling the portfolio

The PATH team compiled a list of more than 70 diagnostics companies based on internal knowledge, discussions with GSK, the landscape evaluation, market research, and patent searches. They then narrowed the list of companies based on perceived ability to achieve technical and commercial success and on factors such as existing complementary technologies, experience in diagnostics in a relevant disease area, freedom to operate, regulatory experience, commercialization infrastructure, and strategy that is aligned with the goals of the PDP. The team reached out to the top 20 companies on the list and conducted face-to-face discussions.

The PATH team entered into confidential discussions with 10 of the 20 companies, 6 of which created significantly advanced product concepts or had sophisticated enough research and development (R&D) capacity to engage rapidly. These companies were invited to present letters of interest for ESAC review.

By the end of 2014, the PDP was advancing early-stage development of three G6PD diagnostic tests, two quantitative and one qualitative. Of the 2 companies working on a quantitative test, 1 was small (Company A) and the other was a major multinational medical technology company (Company B). The company developing the qualitative test was a small R&D company (Company C).

Company A required significant oversight and guidance during the feasibility and proof-of-concept phase, leading to concerns about facing



PATH staff train community health workers in Vietnam on how to interpret G6PD diagnostic tests and record results.

downstream risks for commercialization and ability to meet projected timelines. Its product did not pass technical requirements in the stage gate in 2016. After an attempt to revive this technology with a different partner, the effort was discontinued, and the product was removed from the portfolio.

In 2016, the two remaining tests—one quantitative and one qualitative—passed their stage gates and transitioned to the product development phase.

PATH completed an initial usability study of Company B's quantitative test in 2016 in Thailand, near the Burmese border, which was an important step in better understanding the challenges of using the test and interpreting the results. Usability evaluations throughout the product development process identified areas where users could easily make mistakes. Risks identified through this process were addressed in future product versions or through improved training materials and job aids.

**Early alignment with donors on a portfolio-based approach allowed the PDP to more efficiently pivot to new investments as needed.**

## LESSONS LEARNED EARLY IN THE PDP

### Ensure flexible funding

The PATH team had the flexibility to collaborate with any G6PD test developer, even those outside its portfolio, and to pursue new ideas or potential partners as they emerged. The project was company agnostic—it did not matter who made the product, as long as it met the technical and commercialization requirements.

### Align expectations early in the process

This includes ensuring that companies and funders understand the technical risks, the time it may take to develop and commercialize a product, and the low margins and low volumes involved in global health products.

### Create a rigorous governance structure at the outset

The PATH team held monthly meetings with teams from each partner company to ensure that they were receiving the support they needed, risks were identified early, their products were meeting standards, and collaboration and communication were happening smoothly. The ESAC provided important feedback at key project milestones. Communication with funders around key decisions was likewise structured and deliberate. (See “Resources” at the end for more details on the governance structure.)

### Remain focused on the business case

Just because a product works does not mean there will be a market for it. The PATH project's portfolio included products that failed to advance due to commercialization risk as well as products that had technical problems. The project team should include ample in-house expertise in working with suppliers, determining appropriate pricing, and assessing market needs.

### Conduct early and regular usability testing

Such tests helped identify, for example, whether users of the quantitative test understood how to hold the blood transfer device and which numbers to read as the results. In some cases, the findings led to the inclusion of helpful pictures in the training materials and user guides.

### Verify performance claims at every stage

PATH's in-house testing of the prototype devices generated valuable information that the companies could use to make iterative improvements and helped the project team identify which development efforts were unlikely to meet performance requirements.

### Develop an array of resources to support product developers and the PDP team

The combination of PATH's market analysis, specimen repository, and ability to independently evaluate products was crucial to the project's success and the team's ability to pivot from product to product quickly and support developers as needed along the way.

Due to the disappointing performance of Company A's product and some anticipated challenges with Company B's likely end-user price, the PATH team conducted outreach to other potential partners. They identified one new quantitative G6PD test already in development by a Korea-based diagnostics company, SD Biosensor, and provided support to enable alignment with the PATH TPP, as well as access to

samples in PATH's G6PD repository (see the sidebar on the next page) and market intelligence.

This was the one of several instances in which the early alignment with donors on a portfolio-based approach allowed the PDP to more efficiently pivot to new investments as needed.

# PATH's R&D support

Three assets enabled the PATH team to accelerate progress and reduce the costs associated with feasibility studies and validation, further reducing the commercialization risk of product development efforts for G6PD testing. These assets were available throughout the project.



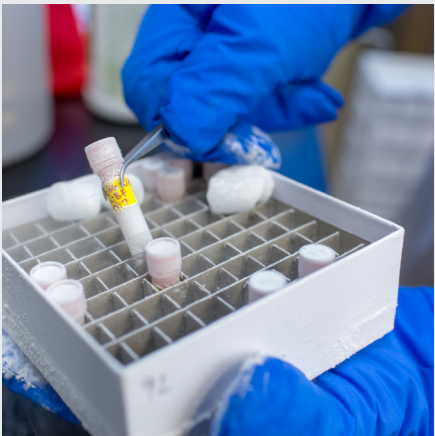
## A gold-standard reference assay

PATH identified an existing lab assay that was used by PATH and by the diagnostic company laboratories to enable calibration of the diagnostic prototypes. Clinical study sites were trained on how to perform the reference assay to ensure high-quality data for regulatory submissions.



## Independent laboratory evaluations

Designed and conducted by the PATH team, these evaluations used criteria based on the TPP targets and were performed throughout the feasibility and product development phases to provide iterative feedback to the developers on areas for improvement. The PATH team also conducted an evaluation at the end of each phase to validate the performance claims of the manufacturers. This evaluation became a key component of each stage gate.



## A specimen repository

The PATH team established a repository containing blood specimens with a range of G6PD deficiency levels characterized by gold-standard G6PD laboratory assays and used them to evaluate performance of the technologies as they progressed through the product development stages. The panels of specimens were also made available free of charge to any company developing a G6PD test. Collecting, processing, and maintaining such a supply of samples would be extremely costly and time-consuming for an individual company.

Photos, left to right: PATH, PATH/Tom Furtwangler, PATH/Christopher Nelson

# Progress and setbacks

In 2017, SD Biosensor's test was registered in India and Thailand, becoming the first quantitative G6PD point-of-care test available in a malaria-endemic country. With PATH support, the company prepared for clinical evaluations to enable WHO prequalification, regulatory approval, and registration in high-priority countries, as well as approval from Australia's Therapeutic Goods Administration (a WHO-recognized SRA).

Company B's quantitative test, previously the lead product in the portfolio, became a backup technology, due primarily to lack of alignment

around commercialization rather than technical issues. When agreement could not be reached on the commercialization terms, the partnership was terminated in 2018. PATH retained the IP per the PDP agreement with Company B.

Company C prepared its product for a technology transfer to a diagnostics manufacturer, but the transfer fell through after the manufacturer was acquired by another company. This was a setback for the product and resulted in Company C continuing to refine the performance of its qualitative test and seeking other manufacturing partners.

## LESSONS LEARNED MIDWAY THROUGH THE PDP

### Seek right-size partners

Larger companies may actually be more risk averse, while smaller companies, including those with less commercialization experience, might be more willing to share risk. They may also accept a smaller profit margin if the noneconomic incentives are attractive—such as the opportunity to build their brand in the global health sector, gain access to new markets, and connect with new partners. It is essential to identify companies with business models that can accommodate small-volume, low-profit product lines to ensure long-term sustainability.

### Seek partners that strategically align with your mission

Ideally, the project fits within the partner company's core business model rather than residing within its social corporate responsibility department. This will ensure that the company has incentive to share some financial risk, particularly for commercialization. Companies with a strong package of complementary products might be more motivated because the new product will add to the value they already offer in the marketplace with an incremental increase in cost.

### Collaborate with impartial experts for objective decision-making

The ESAC, which included members with expertise in G6PD deficiency, product development, blood disorders, and other relevant areas, met at least once a year to provide independent, real-world insight that aided in objective decision-making, particularly at the stage gates. Their perspective was instrumental in the decision to discontinue work with a company after the PATH team had spent significant time, energy, and funding on those partnerships.

### Remain objective—use data and metrics to assess the status of each partnership

Bias and emotion can lead to unrealistic hopes or inability to recognize that a partnership should not advance to the next stage. The Probability of Success tool developed by the PATH team (described in "Resource B"), along with other analytics used throughout the project, helped the team objectively assess the status of each partnership. Early on, this tool clearly showed that advancing only one candidate would have a low probability of a product reaching commercial launch, even if it were to meet all of the technical criteria. This helped support the decision to maintain a portfolio even after SD Biosensor had a commercial product.



# A more streamlined portfolio

In 2018, coinciding with the introduction of tafenoquine, SD Biosensor’s quantitative test was registered in three additional malaria-endemic countries: Brazil, Indonesia, and Myanmar.

The PATH team continued to pursue transfer of Company B’s technology to increase the likelihood of another high-quality test reaching the market. It identified a diagnostics manufacturer in China, Wondfo Biotech, and a transfer was concluded in 2020. Wondfo did additional R&D and created prototypes for PATH evaluation. As of 2021, it has passed the feasibility stage-gate process to advance through product development to the clinical study stage gate.

By 2021, SD Biosensor’s test was being distributed to 30 countries worldwide, reaching populations most in need of point-of-care G6PD testing. In April 2021, the test received regulatory approval from the Australian Therapeutic Goods Administration. Cambodia, Laos, and Vietnam are introducing routine use of the test with primaquine. In Cambodia, the test has enabled

equal access to radical cure of *P. vivax* malaria to both males and females for the first time.

In the meantime, performance issues with Company C’s qualitative test and lack of a manufacturing partner led PATH to suspend further development of that test. In parallel, the PATH team began evaluating and providing feedback on development of two other qualitative tests, one from a Korea-based company and one from a US-based company.

As of 2021, the PATH team continued to work with global and in-country partners to increase access to the SD Biosensor STANDARD™ G6PD test. As new tests come to market, PATH will support and guide manufacturers to facilitate test registration, manufacture, and sale in countries where the tests are needed most.

Figure 2 shows the project trajectory from 2014 to 2021 and highlights the importance of having a portfolio of products, given that development of several products was discontinued along the way for commercial or technical reasons.

## LESSONS LEARNED LATER IN THE PDP

### Consider technologies at any stage of development

Valuable technologies may be found anywhere along the product development cycle, from the early R&D stage to an already commercialized product.

### Conduct due diligence on all potential partners

This includes ensuring that companies have not only the technical and commercialization expertise they claim to have but also a business model that truly aligns with the project and sufficient incentives to share risk. Due diligence should be repeated when significant change occurs at the company, such as key staff leaving or corporate strategy shifting.

### Ensure broad expertise on the project team

The PATH team included a project manager, a scientific lead, public health officers, technical officers, commercialization officers, laboratory staff,

and finance and administration staff. This breadth of knowledge supporting the project was critical to identifying and mitigating risks as they emerged.

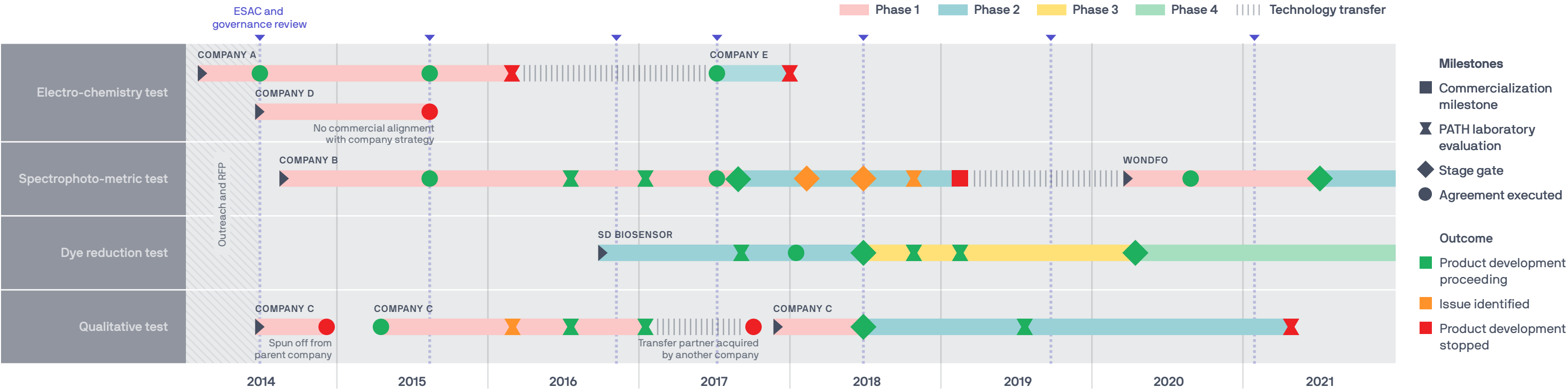
### Ensure robust project management

The project management function is crucial because the project manager moves the project forward, ensures that milestones are met, reminds team members of overall goals as well as decisions that have already been made, and keeps the team focused on shared criteria for decision-making.

### Develop shared plans and timelines with each partner for each stage

The team worked with each product development company to create an integrated product development plan that included a technical development plan, a regulatory plan, and a commercialization plan. All were updated before each stage gate.

FIGURE 2. G6PD Diagnostic Initiative portfolio trajectory, 2014–2021.





# PDPs: looking ahead

The G6PD Diagnostic Initiative encompasses a very dynamic portfolio with several products stalling, stopping, restarting, or joining late. This has required hands-on, proactive project management and the creation of several tools to help evaluate risk, create cost projections, and facilitate objective decision-making about which partners and products merit continued investment (see “Resources”). Had the portfolio been unable to include multiple products and continue identifying new products, it would have taken significantly longer to reach a commercialized G6PD test. None of the initial products selected for investment has reached the commercialization stage—two failed for technical reasons and one

To learn more about PATH’s G6PD Diagnostic Initiative, visit [www.path.org/programs/diagnostics/malaria-diagnostics/](http://www.path.org/programs/diagnostics/malaria-diagnostics/).

was transferred to another company due to the lack of alignment on commercialization terms with the original company.

Fortunately, the flexibility offered by this approach allowed the team to continually pivot to new products, one of which is the SD Biosensor STANDARD™ G6PD test, which is already being adopted for its intended use. Wondfo Biotech continues to advance the G6PD test based on the transferred technology. The PDP continues to monitor the G6PD test landscape and support product development of the remaining products in the portfolio to ensure that there are sufficient suppliers of G6PD point-of-care tests.

Investments in clinical development of health products will always have a high risk of failure, and PDPs offer a way to share that risk and proactively manage it. By pooling funds from multiple sources—public, private, and philanthropic—and taking a portfolio-based approach, PDPs are not only accelerating the development of life-saving products but also building the capacity and expertise of manufacturers, researchers, and clinical study sites. Those benefits will lead to stronger health systems that can better respond to future health needs.



The Standard G6PD is the first commercialized test to result from the PDP and is available in several low -and- middle income countries.

# Resources

## Resource A: Lessons learned

The PATH team’s experience shows that robust systems and tools are crucial to increasing the likelihood that at least one successful product meeting the global health need will come to market. The success of the G6PD Diagnostic Initiative ultimately hinged on pursuing several lead candidates at once to provide a better chance of success in a minimal amount of time, as well as maintaining a pipeline of preclinical and early-stage

candidates that could be advanced if a lead candidate failed. Equally important were the use of stage gates as decision points for advancing or eliminating candidates and use of analytics to determine the probability that a candidate would make it to each stage gate.

The PATH team identified the following key lessons from the project that may be applicable to other portfolio-based PDP efforts for global health. They are organized here by category.

## Assembling a portfolio

### Ensure flexible funding

The PATH team had the flexibility to collaborate with any G6PD test developer, even those outside its portfolio, and to pursue new ideas or potential partners as they emerged. The project was company agnostic—it did not matter who made the product, as long as it met the technical and commercialization requirements.

### Consider technologies at any stage of development

Valuable technologies may be found anywhere along the product development cycle, from the early R&D stage to an already commercialized product.

### Conduct early and regular usability testing

Such tests helped identify, for example, whether users of the quantitative test understood how to hold the blood transfer device and which numbers to read as the results. In some cases, the findings led to the inclusion of helpful pictures in the training materials and user guides.

### Verify performance claims at every stage

PATH’s in-house testing of the prototype devices generated valuable information that the companies could use to make iterative improvements and helped the project team identify which development efforts were unlikely to meet performance requirements.

Seeking partners

Seek partners that strategically align with your mission

Ideally, the project fits within the partner company’s core business model rather than residing within its social corporate responsibility department. This will ensure that the company has incentive to share some financial risk, particularly for commercialization. Companies with a strong package of complementary products might be more motivated because the new product will add to the value they already offer in the marketplace with an incremental increase in cost.

Seek right-size partners

Larger companies may actually be more risk averse, while smaller companies, including those with less commercialization experience, might be more willing to share risk. They may also accept a smaller profit margin if the noneconomic incentives are attractive—such as the opportunity to build their brand in the global health sector, gain access to new markets, and connect with new partners. It is essential to identify companies with business models that can accommodate small-volume, low-profit product lines to ensure long-term sustainability.

Conduct due diligence on all potential partners

This includes ensuring that companies have not only the technical and commercialization expertise they claim to have but also a business model that truly aligns with the project and sufficient incentives to share risk. Due diligence should be repeated when significant change occurs at the company, such as key staff leaving or corporate strategy shifting.

Remain focused on the business case

Just because a product works does not mean there will be a market for it. The PATH project’s portfolio included products that failed to advance due to commercialization risk as well as products that had technical problems. The project team should include ample in-house expertise in working with suppliers, determining appropriate pricing, and assessing market needs.

Managing the PDP

Align expectations early in the process

This includes ensuring that companies and funders understand the technical risks, the time it may take to develop and commercialize a product, and the low margins and low volumes involved in global health products.

Develop shared plans and timelines with each partner for each stage

The team worked with each product development company to create an integrated product development plan that included a technical development plan, a regulatory plan, and a commercialization plan. All were updated before each stage gate.

Ensure broad expertise on the project team

The PATH team included a project manager, a scientific lead, public health officers, technical officers, commercialization officers, laboratory staff, and finance and administration staff. This breadth of knowledge supporting the project was critical to identifying and mitigating risks as they emerged.

Ensure robust project management

The project management function is crucial because the project manager moves the project forward, ensures that milestones are met, reminds team members of overall goals as well as decisions that have already been made, and keeps the team focused on shared criteria for decision-making.

Develop an array of resources to support product developers and the PDP team

The combination of PATH’s market analysis, specimen repository, and ability to independently evaluate products was crucial to the project’s success and the team’s ability to pivot from product to product quickly and support developers as needed along the way.

Create a rigorous governance structure at the outset

The PATH team held monthly meetings with teams from each partner company to ensure that they were receiving the support they needed, risks were identified early, their products were meeting standards, and collaboration and communication were happening smoothly. The ESAC provided important feedback at key project milestones. Communication with funders around key decisions was likewise structured and deliberate.

Collaborate with impartial experts for objective decision-making

The ESAC, which included members with expertise in G6PD deficiency, product development, blood disorders, and other relevant areas, met at least once a year to provide independent, real-world insight that aided in objective decision-making, particularly at the stage gates. Their perspective was instrumental in the decision to discontinue work with a company after the PATH team had spent significant time, energy, and funding on those partnerships.

Remain objective—use data and metrics to assess the status of each partnership

Bias and emotion can lead to unrealistic hopes or inability to recognize that a partnership should not advance to the next stage. The Probability of Success tool developed by the PATH team (described in the “Resource B”), along with other analytics used throughout the project, helped the team objectively assess the status of each partnership. Early on, this tool clearly showed that advancing only one candidate would have a low probability of a product reaching commercial launch, even if it were to meet all of the technical criteria. This helped support the decision to maintain a portfolio even after SD Biosensor had a commercial product.



Resource B: Probability of Success tool

The PATH team’s Probability of Success tool established assessment criteria for each product development phase, including manufacturing and launch. PATH team members who were most familiar with each product candidate assigned a score of high, medium, or low for that product on each criterion. The qualitative scale was then converted to a fixed quantitative scale, and the scores were averaged. Where scores diverged, the team members

discussed them and came to a consensus. An equal weighted average score across all criteria in a phase was calculated for each partner and was used as a proxy for its probability of success.

Figures B-1 and B-2 show visualizations from the Probability of Success tool, with three product candidates in the portfolio. These are depicted for illustrative purposes but are based on actual companies whose names have been anonymized.

FIGURE B-1. Comparative probability of success scores for three companies.

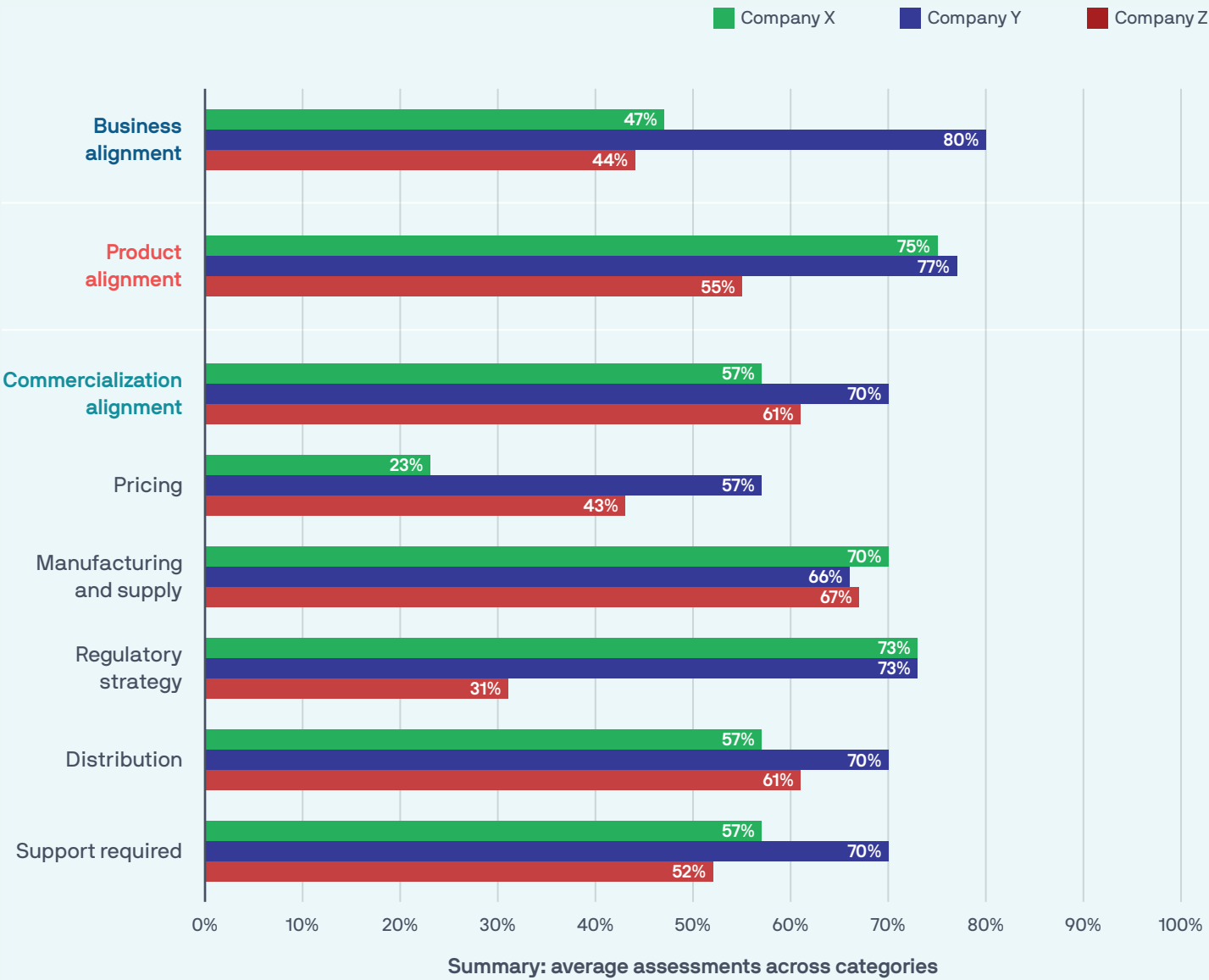
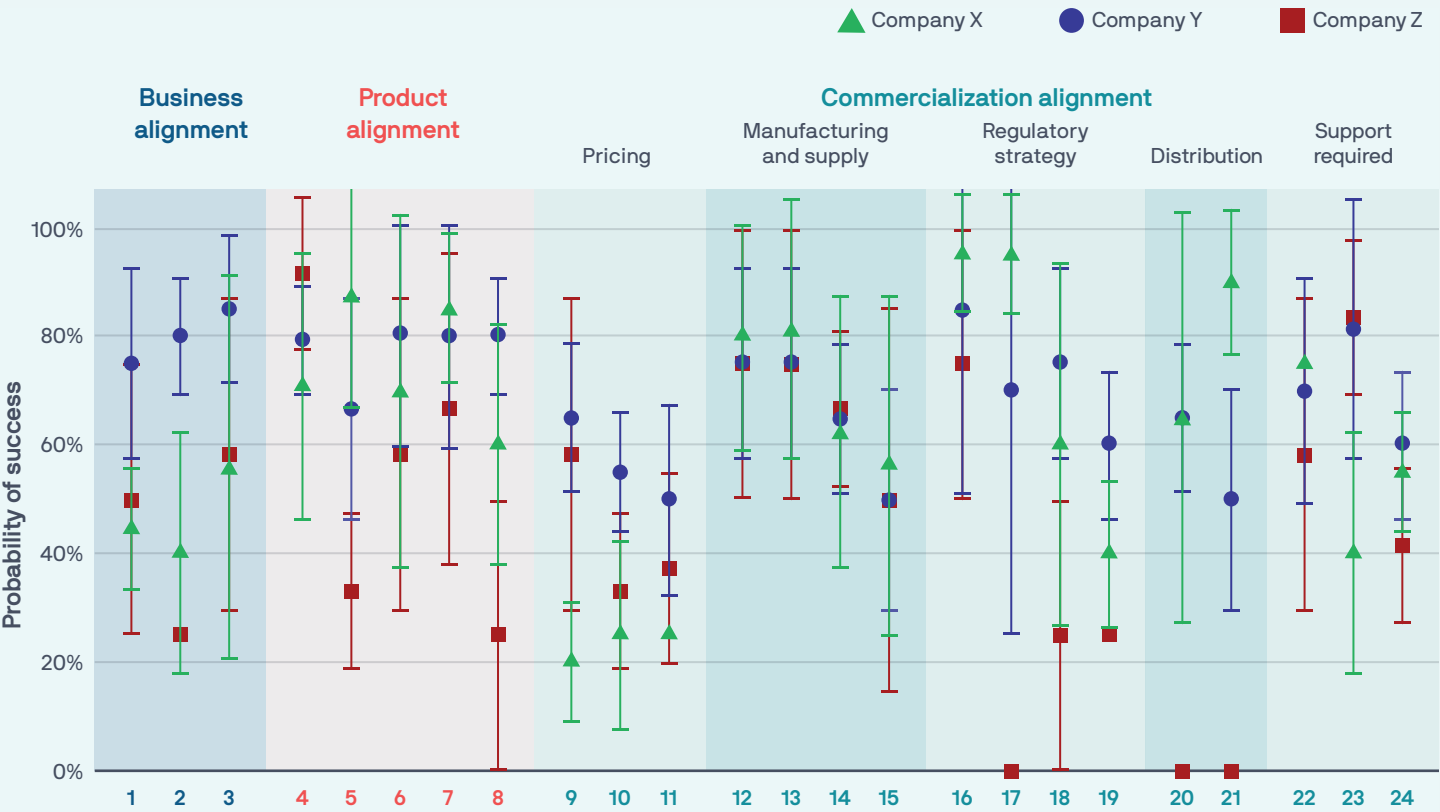


FIGURE B-2. Another comparative view of the probability of success scores for three companies.



Business alignment

1. G6PD project aligns with company's strategy, potentially strengthens its financial outlook, and/or aligns with its internal mission or corporate social responsibility goals
2. Company is internally motivated to support the project
3. Supporting the project goals will help, not hurt, company's overall business

Product alignment

4. Company's product meets the TPP usability / access specifications
5. Company's product meets TPP analytical performance specifications
6. Company's product meets other TPP specifications
7. Product concept is conducive to receiving SRA approval
8. Company's product development timeline supports the project timeline

Commercialization alignment

Pricing

9. Projected cost of goods is conducive to meeting TPP pricing
10. Company is committed to accepting reasonable profit margins on the product
11. Company is committed to meeting the TPP price

Manufacturing and supply

12. Company can manufacture the product to appropriate quality standards
13. Company has or will have sufficient manufacturing capacity to meet demand
14. Company has ability to cost-effectively scale up production to meet demand
15. Company turnaround time for processing orders is reasonable

Regulatory strategy

16. Company has SRA experience (Food and Drug Administration, European Medicines Agency)
17. Company has WHO prequalification experience
18. Company is committed to registering in target countries
19. Company is capable of meeting regulatory timelines

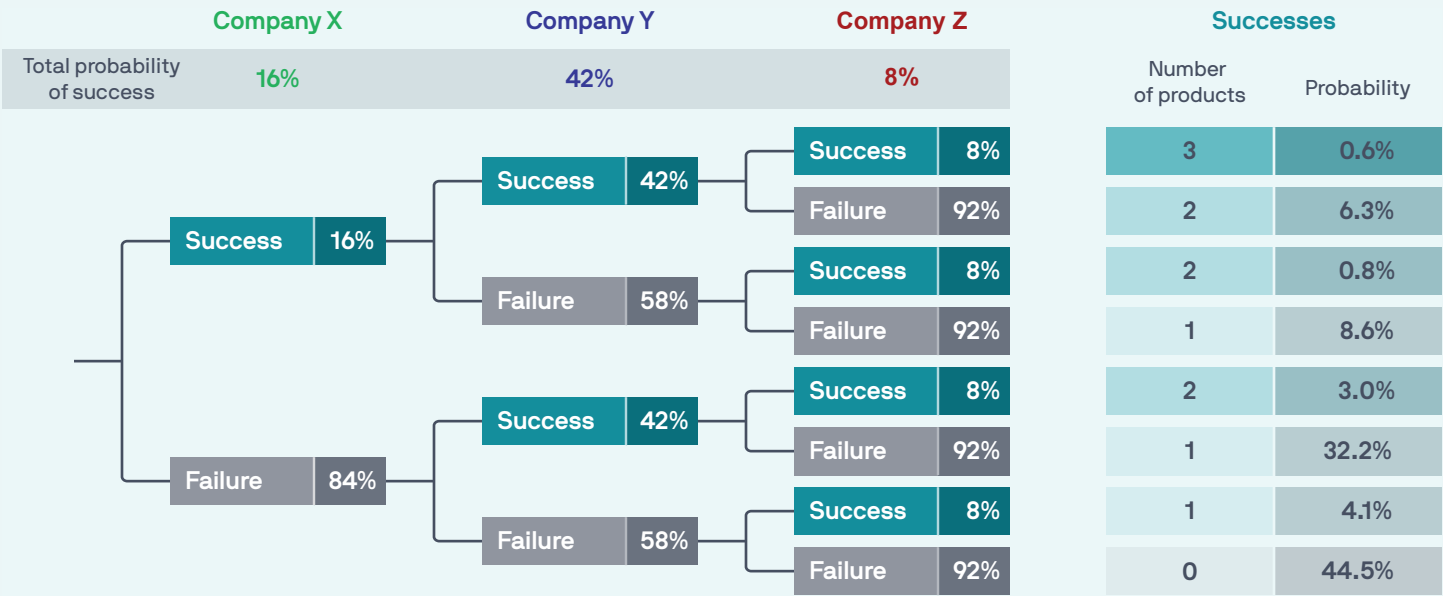
Distribution

20. Company has an active distribution network in target geographies
21. Company has experience with public-sector distribution in developing countries

Support required

22. Technical assistance required by company is reasonable and within the project scope
23. Resources required by company are reasonable and within the project scope
24. Overall, company is a good fit for meeting the needs of the project

FIGURE B-3. Cumulative probability of success for a portfolio of three companies.



Probability of successful commercialization\*

With three product candidates in the portfolio, there are a total of eight outcome permutations based on a binary “success/failure” assessment for each individual product. Based on the probability of success assessment for each individual product, a total portfolio probability of success can be calculated. In this case, it was calculated that the probability of commercial success of one or more products was 56% for the entire portfolio.

Number of products	Probability of occurrence	Number of products	Cumulative probability
3	1%	3	1%
2	10%	2 or more	11%
1	45%	1 or more	56%
0	44%		

\*Commercialization=stringent regulatory authority approval, WHO prequalification, and registration and sale in at least three target countries.

After assessing the individual product candidates, the PATH team conducted a probability of success analysis at the portfolio level. Figure B-3 shows eight potential outcomes with three products in the portfolio. With all of the individual probabilities considered, the total probability that at least one product would be successfully commercialized was 56 percent. (Note that this probability was not tied to a specific product being commercialized but rather to any one or more products from the portfolio being successfully commercialized if the portfolio of three products was maintained.) Commercial success was defined as SRA approval, WHO prequalification, and registration and sale in at least three target countries.

The probability of success was further analyzed by product development phases. This analysis helped guide investment decisions about when and where to apply resources to increase the overall probability of success of the portfolio. The move from phase 3 to regulatory approval accounted for one of the largest dips in the overall probability of success of the portfolio. This helped guide additional investments in the form of resources and technical assistance to support companies with regulatory dossier development and submissions.

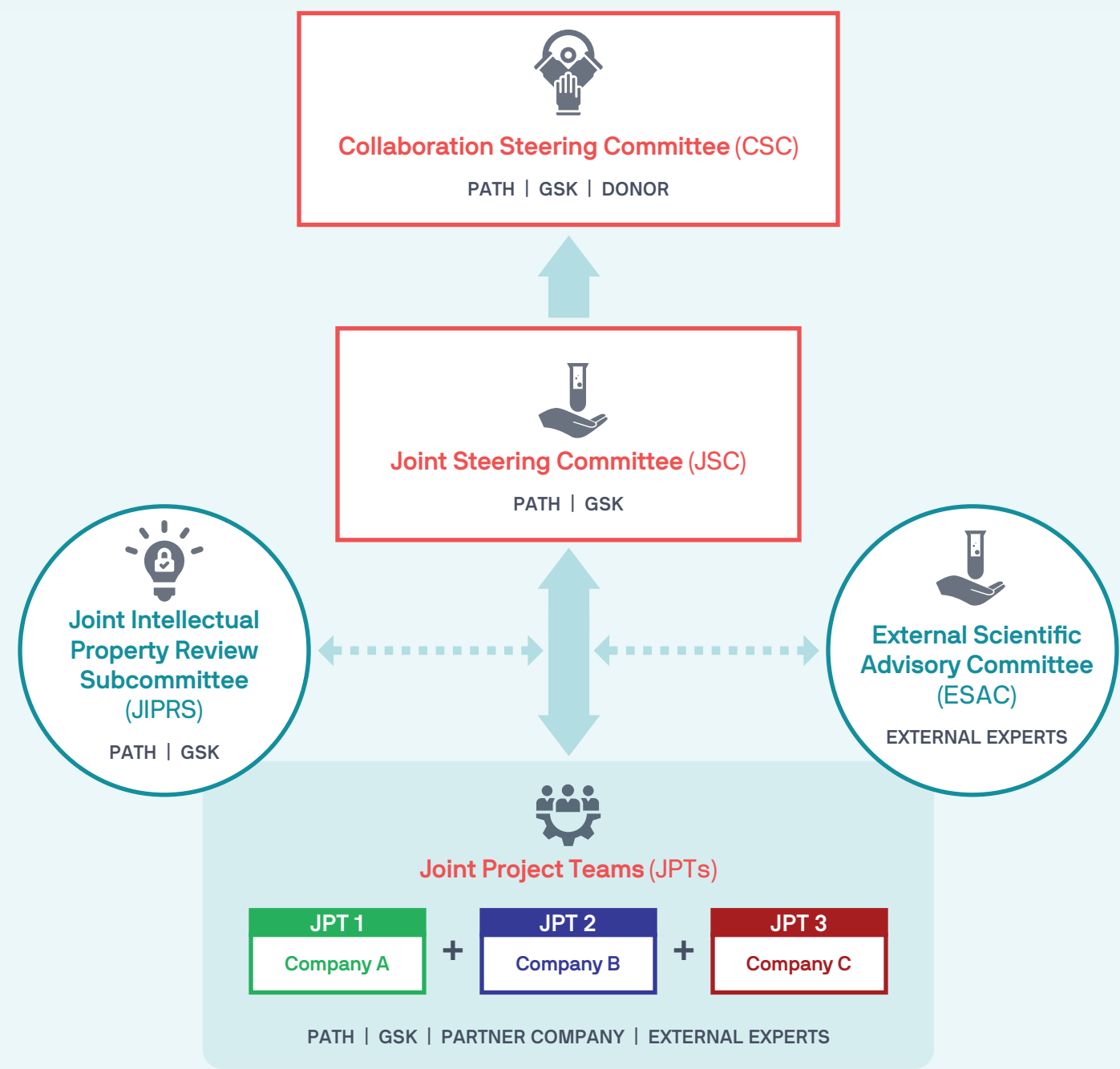


Resource C: Governance structure

The PDP established a governance structure at the outset of the project to ensure consistent governance and key stakeholder input, modeled on the governance model used by Medicines for Malaria Venture for its PDPs. The committees and subcommittees are listed below, along with their

roles, responsibilities, and membership. Figure C-1 depicts the flow of information to the final decision-making body, the Collaboration Steering Committee. PATH and GSK held additional working meetings outside the formal governance structure to ensure strong coordination and collaboration.

FIGURE C-1. G6PD Diagnostic Initiative governance structure.



Collaboration Steering Committee (CSC)

The CSC was the final decision-making body that would review inputs from all other committees and endorse financial investments in the products. Committee members were composed of senior leadership at GSK and PATH and the PDP donors.

- Key responsibilities:**
- Endorse members for the ESAC
  - Endorse recommendations from the Joint Steering Committee (JSC) on product development strategy
  - Endorse/approve recommendations from the JSC on which companies to fund

- Meetings:**
- At least once every six months, ideally in person
- Members:**
- GSK and PATH leadership, with the chair alternating between GSK, PATH, and the donor
- Decision-making:**
- Unanimous

Joint Steering Committee (JSC)

The JSC had an equal number of voting members from each organization; this allowed the PATH team to formally recommend decisions or actions for the portfolio that could be escalated to the CSC level for approval. When products neared the end of a development phase or issues needed to be escalated to determine next steps, a JSC meeting could be called. Otherwise, meetings took place on an as-needed basis.

- Key responsibilities:**
- Provide strategic oversight of the G6PD Diagnostic Initiative
  - Make recommendations to the CSC on which companies to fund (and the amount), taking into account ESAC and JIPRS recommendations
  - Approve contracts between GSK, PATH, and product development companies
  - Coordinate the relationship and flow of information between PATH and GSK
  - Manage relationships with the product development companies
  - Make all strategic decisions relating to the collaboration

- Meetings:**
- As needed, but at least twice a year, with at least one of those an in-person meeting
- Members:**
- Project team leadership; chair alternating between GSK and PATH, starting with GSK
- Decision-making:**
- Unanimous

Joint Project Teams (JPTs)

One per product development company

Joint project team meetings were crucial for understanding how each product was progressing and provided opportunities to troubleshoot or escalate issues and determine next steps. These meetings established a way of working with a new product development company from the outset of the partnership.

Key responsibilities:

- Provide oversight of product development for a given company
- Provide project management and risk management for each product development effort

Meetings:

- Monthly

Members:

- Project team members and representatives from PATH, GSK, and the company

Decision-making:

- Unanimous

Joint Intellectual Property Review Subcommittee (JIPRS)

This subcommittee reviewed potential patent filings and ensured that all the product designs were not infringing on any existing patents. This subcommittee was rarely convened because few IP issues arose that warranted escalation to this level.

Key responsibility:

- Advise the JSC on any IP issues

Meetings:

- As needed

Members:

- One senior representative (or consultant) with IP experience each from GSK and PATH

Decision-making:

- Unanimous

External Scientific Advisory Committee (ESAC)

The ESAC conducted an annual review of the entire portfolio and provided recommendations on additional testing that needed to be performed, regulatory considerations, and end-user considerations. These scientific experts provided diverse perspectives and valuable insights to ground the portfolio in real-world expectations.

Key responsibilities:

- Review development plans and progress of diagnostic products
- Make recommendations to the JSC on granting additional funding to companies for further product development and advancing products to field evaluation

Meetings:

- Annual in-person meeting and phone/email communications as needed

Members:

- External experts in diagnostics, hematology, public health, malaria, and other relevant fields; JSC-selected chair

References

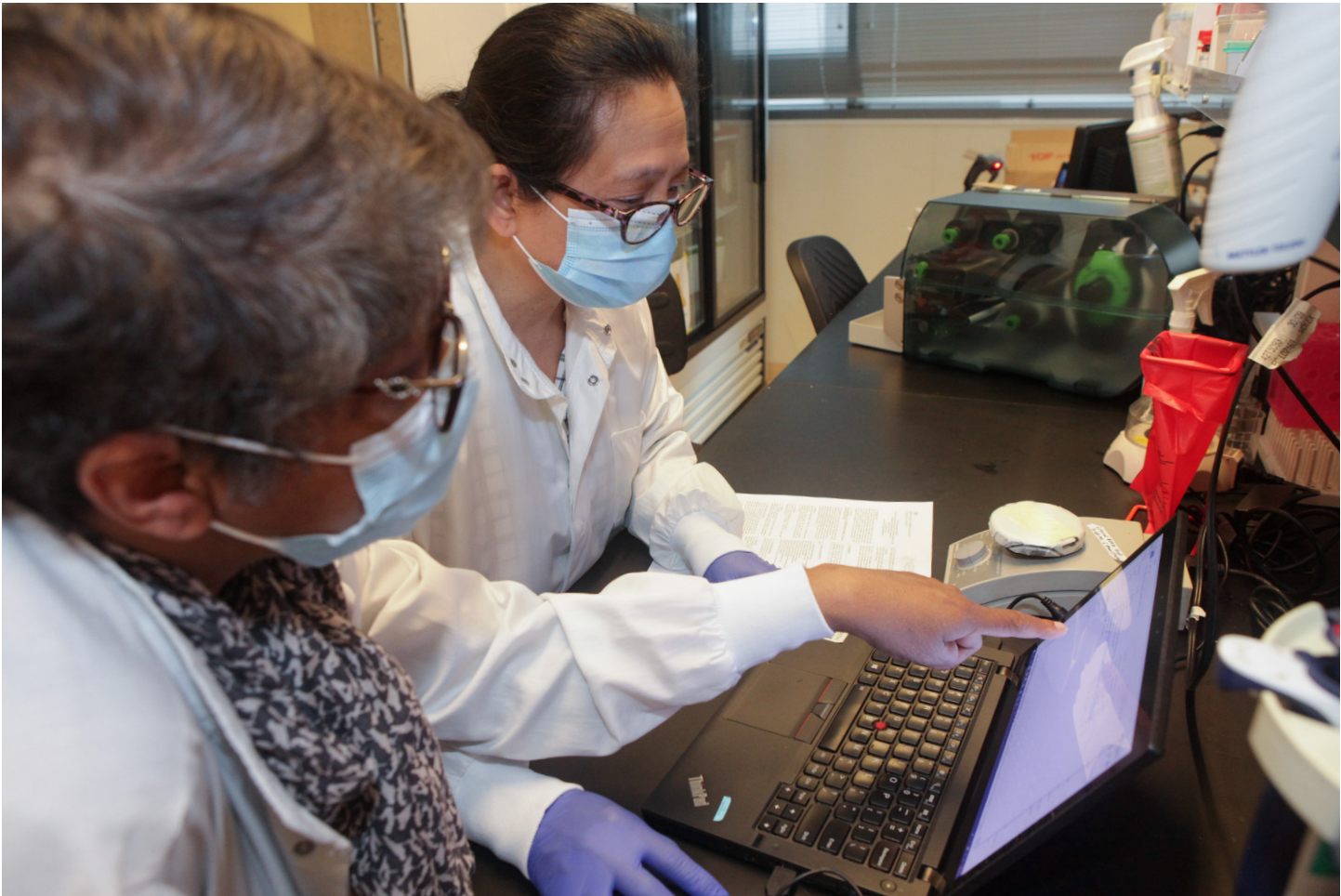
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PATH laboratory team review the data from a G6PD test evaluation.



