INNOVATION CASE STUDY

November 2019

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for every child

Zika Virus Diagnostics for Testing at Point-of-Care

EVALUATION OFFICE

Evaluation of Innovation in UNICEF Work
Case Study: Zika Virus Diagnostics for Testing at Point-of-Care

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This case study report for the Zika Virus (ZIKV) Diagnostics for Testing at Point-of-Care is one of thirteen innovation case studies which were conducted as part of a global evaluation titled 'Evaluation of innovation in UNICEF work'. The case study component of the evaluation was conducted by Deloitte LLC. The ZIKV Diagnostics for Testing at Point-of-Care case study report was prepared by Edward Thomas, Katherine Arblaster, Ariel Kangasniemi, Laura Maxwell and Adarsh Desai. Beth Plowman, Senior Evaluation Specialist, Evaluation Office, led and managed the overall evaluation process in close collaboration with the Supply Division.

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LIST OF ACRONYMS

Ab	Antibody
Ag	Antigen
ANVISA	Brazil Agência Nacional de Vigilância Sanitária
APC	Advance Purchase Commitment
CDC	United States Centers for Disease Control and Prevention
CE	Conformité Européene
CO	Country Office
EO	Evaluation Office
EUA	Emergency Use Authorization
EUAL	Emergency Use Assessment and Listing
HTC	Health Technology Centre in Supply Division
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IgM-ELISA	IgM Enzyme-linked Immunosorbent Assay
IRB	Innovation Review Board
IVD	In Vitro Diagnostic
LACRO	Latin America and the Caribbean Regional Office
LTA	Long-Term Arrangement
LSHTM	London School of Hygiene and Tropical Medicine
MFSDU	Markets, Finance, and Strategic Data Unit in Supply Division
PAHO	Pan American Health Organization
POC	Point of Care
PRG	Procurement Reference Group
PIP	Product Innovation Project
QA	Quality Assurance
QMS	Quality Management System
R&D	Research and Development
RDT	Rapid Diagnostic Test
RFP	Request for Proposal
SD	Supply Division
IU	Supply Division Innovation Unit
SRA	Stringent Regulatory Authority
SRP	Strategy Response Plan
TPP	Target Product Profile
USAID	The United States Agency for International Development
US FDA	United States Food and Drug Administration
WHO	World Health Organization
ZIKV Dx	ZIKV in Vitro Diagnostics
ZIKV	Zika Virus

EXECUTIVE SUMMARY

Since 2014, UNICEF has embraced innovation as one of its key strategies to achieve results for children. That commitment is reaffirmed in its current Strategic Plan, 2018-2021, and is evident in the organization's programming and institutional architecture. Indeed, since 2014, significant progress has occurred in a relatively short period of time, backed by clear strategic intent and targeted investment. With the increased foothold of innovation in UNICEF, it is important and timely to take stock of these efforts through high quality evidence to inform decision-making, learning and accountability. In keeping with the need for this evidence, UNICEF conducted an global evaluation of innovation in 2018.

The objective of the global evaluation was to assess UNICEF's 'fitness for purpose' to employ innovation as a key strategy to achieve the outcomes and goals defined in its strategic plans covering the period 2014-2021. A set of innovation case studies was a key element of this global evaluation, along with an organizational assessment and a synthesis project. The case studies were guided by three objectives:

- To provide detailed descriptions of a set of innovations across stages of the development continuum inclusive of contextual influences
- To assess the application of innovation principles or other standards for a set of innovations with particular attention to issues of ownership and scale
- To produce clear conclusions and considerations for policy, strategy and management decisions to further enhance innovation as key change strategy.

Case studies were conducted by Deloitte LLP over the period February 2018-January 2019. Mixed methods were utilized for data collection including key informant interviews, document review and observations in the field.

The innovation case examined in this report concerns the ZIKV Diagnostics for Testing at Point-of-Care. Following an outbreak of Zika virus (ZIKV) in Southern America in 2015, the UNICEF Supply Division (SD) identified the need for a rapid diagnostic test (RDT) that could be used at the point of care (POC) to diagnose infection and for surveillance purposes. The rapid ZIKV Diagnostics (Dx) project is intended to accelerate development and commercial availability of diagnostics that are accurate (i.e., sensitive and specific), rapid and low cost, and that can be used at POC in low-resource settings. SD, the Pan American Health Organization (PAHO), FIND and the World Health Organization (WHO) developed a Target Product Profile (TPP) to communicate a set of required and ideal product characteristics to guide industry to develop diagnostics to meet these needs. Further, SD and the United States Agency of International Development (USAID) designed an Advance Purchase Commitment (APC) to incentivize product development. The design was such that through a competitive Request for Proposal (RFP) process, SD would award manufacturers long-term agreements (LTAs) for procurement of their diagnostic, including an APC guaranteeing off-take for a portion of the forecasted amount of product to be procured regardless of the materialization of demand.

The Project Team is responsible for day-to-day decision-making for the project and has included membership from the Health Technology Centre (HTC), Innovation Unit (IU), and Markets, Finance and Strategic Data Unit (MFSDU), depending on the phase of the project and expertise required. The project has received significant support and buy-in from SD leadership, including encouragement from the Director's Office to get involved in the response to the epidemic, and guidance from the Innovation Review Board (IRB); the decision-making body in the Product Innovation Project (PIP) process, including leadership-level membership. The stage-gated process followed for innovation projects provides entry points for guidance and insight from industry, the IRB and the Procurement Reference Group (PRG); and technical experts that provide direction and support to the Project Team over the life cycle of the innovation.

USAID funded a US$10 million APC to incentivize product development. The APC is the first of its kind for UNICEF and USAID, in response to the emergency status of the outbreak and international pressure to respond. The estimated project budget in 2016 was between US$247,109 and US$823,339 and included staff salaries, travel and expenses, a two-day supplier conference, and field trials. As of December 2018, financial values for the complete project are not available. The Project Team is able to leverage expertise and capabilities from various units and centres within SD, complemented by advisory input from the PRG and services from the London School of Hygiene and Tropical Medicine (LSHTM), which will leverage its network of specimen collection sites to complete the clinical evaluations of selected diagnostics on behalf of UNICEF.

To incentivize investment in research and development (R&D) of rapid ZIKV Dx, USAID provided funding to establish an APC to guarantee procurement of a certain quantity of product from manufacturers, de-risking product development. While diagnostics selected in the first tender process were already in development prior to launching the RFP, manufacturers were able to refine product design and ensure that products were user-friendly for users with limited access to training and/or sophisticated technical equipment, based on guidance provided in the TPP. Six manufacturers responded to the first tender, from which UNICEF awarded two products 36-month LTAs.

Teams considering initiating an innovation project should take away a number of lessons learned from the innovation pathway of the rapid ZIKV Dx project so far. One of the project's strengths is the diverse membership of the Project Team (e.g., from HTC, IU, MFSDU), which has strengthened its outputs by leveraging expertise from different areas of SD, depending on the phase of the project. However, greater participation at the Regional and Country Office levels, particularly for needs identification and demand generation, could further improve the likelihood of project success. The creation of an internal structure for innovation projects has also been an important component of creating an enabling environment for innovation at SD, and could be replicated for similar innovation projects that involve partnership with external organizations to drive research and development. The methodology developed provides an internal structure for project development and progression through a stage-gated process, while providing manufacturers with the flexibility needed to develop novel products that are fit for purpose and that respond to unmet programme needs through RFPs and TPPs that are less prescriptive.

While the project faced challenges associated with the emergency status of the epidemic and limited understanding of the virus' epidemiology, SD and its partners were able to develop a business case for developing rapid ZIKV Dx through product mapping, identification of gaps, and a demand forecast to demonstrate the need and potential for procurement. The TPP and demand forecast provided an entry point for manufacturers to engage with UNICEF, and an opportunity for industry and academia to provide feedback on the projections and ideal product characteristics, challenging assumptions made by SD. This also served to generate alignment and buy-in across industry.

Another challenge encountered over the course of the project has been the regulatory approval requirements for products prior to procurement. While necessary for new diagnostic products, the approval process has delayed progress towards market availability of products selected for LTAs during the first tender. In response to manufacturer challenges to obtain a well-characterized serum panel to validate their assays, due to the limited availability of serological samples of ZIKV and a lack of commercial panels validated by regulatory authorities, SD has contracted LSHTM to complete clinical evaluations by designing a panel and conducting lab-based validations. Finally, the use of APCs to drive the market towards R&D for novel diagnostic products appears to be working and has been well received by industry. This model could be replicated for similar innovation projects, but its effectiveness in stimulating and/or accelerating development of new products that would otherwise not make it to market should be

reviewed following completion of the second tender.

1. INTRODUCTION

The world is changing faster than ever before, and so too are the challenges facing its most vulnerable. Conflict and displacement, disasters and climate change, urbanization and disease outbreaks are growing increasingly complex and inter-related, demanding new strategies and approaches. Innovation for development – exploring new ways of delivering programmes, with new partners and new technologies – is increasingly recognized as crucial to meeting the Sustainable Development Goals and the promise of the 2030 Agenda for Sustainable Development.

Since 2014, UNICEF embraced innovation as one of its key strategies to achieve results for children. That commitment is reaffirmed in its current Strategic Plan, 2018-2021, and is evident in the organization's programming and institutional architecture. Indeed, since 2014, significant progress has occurred in a relatively short period of time, backed by clear strategic intent and targeted investment. A number of formal structures have evolved, and new milestones achieved.

With the increased foothold of innovation in UNICEF, it is important and timely to take stock of these efforts through high quality evidence to inform decision-making, learning and accountability. In keeping with the need for this evidence, UNICEF conducted an global evaluation of innovation in 2018. The evaluation comes at a time when the organization is considering how best to maximize its resources for innovation and is intended to inform those decisions in an impartial manner, backed by credible evidence.

The objective of the evaluation was to assess UNICEF's 'fitness for purpose' to employ innovation as a key strategy to achieve the outcomes and goals defined in its strategic plans covering the period 2014-2021. It also sought to provide insights on how innovation contributes to UNICEF's goals and objectives, as well as how innovation might contribute to increasingly effective organizational responses in the coming years. The global evaluation was designed with three core components including: an organizational assessment, a set of innovation case studies and a synthesis project.

The case studies are intended to serve organizational learning by unpacking and examining the multiple pathways and dynamics which underpin innovation within the organization. In addition, the case studies contribute to accountability by assessing the manner in which innovation work in practice reflects the strategies and principles which UNICEF has developed to guide these efforts.

Three objectives guided the work:

- To provide detailed descriptions of a set of innovations across stages of the development continuum inclusive of contextual influences
- To assess the application of innovation principles or other standards for a set of innovations with particular attention to issues of ownership and scale
- To produce clear conclusions and considerations for policy, strategy and management decisions to further enhance innovation as key change strategy.

Cases are defined as *the processes an innovation was identified, developed, tested, implemented and taken to scale along with contextual factors such as underlying organizational and partnership arrangements*. The primary audience for the case studies is internal to UNICEF including senior management and programme managers at HQ, regional and country level. Its uses include informing the implementation of the Strategic Plan 2018-2021 particularly the change strategy focused on innovation. UNICEF commissioned Deloitte LLP to conduct thirteen case studies to examine innovation across the spectrum of innovation types, country contexts and internal (UNICEF) and external (partner, supplier) actors.

All case studies were structured around a modified version of the Deloitte Doblin Framework for Innovation. Within this

framework, four thematic dimensions (i.e. approach, organization, resources and capabilities and metrics and incentives) are seen as necessary to enable successful innovation. Case studies employed a mixed methods approach to build a complete picture of the innovation process and identify findings related to these four thematic dimensions. The evaluation team collected qualitative and quantitative data through desktop review, case study informant interviews and field visits. More information on the methods used appears in Annex A. A listing of stakeholders and interviewees appears in Annex B. Documents reviewed appear in Annex C.

The innovation case examined in this report concerns the ZIKV Diagnostics for Testing at Point-of-Care. The project is intended to accelerate development and commercial availability of diagnostics that are accurate (i.e., sensitive and specific), rapid and low cost, and that can be used at POC in low-resource settings. SD, the Pan American Health Organization (PAHO), FIND and the World Health Organization (WHO) developed a Target Product Profile (TPP) to communicate a set of required and ideal product characteristics to guide industry to develop diagnostics to meet these needs. Further, SD and the United States Agency of International Development (USAID) designed an Advance Purchase Commitment (APC) to incentivize product development.

This report includes information on the context for the development of ZIKV Diagnostics (Section 3), the innovation journey (Section 4), findings (Section 5) and considerations for UNICEF and conclusions (Section 6).

2. INNOVATION AT A GLANCE

Zika virus diagnostics

Researchers first identified the Zika virus (ZIKV) in Africa in the 1940s,[1] but little is known about its transmission and association with health conditions including microcephaly and Guillain-Barré syndrome. The issue of limited understanding of ZIKV is compounded by a lack of treatment options and the complexity of available diagnostic tests, which require a specialized and qualified laboratory environment for both molecular and serological testing. To detect ZIKV RNA, testing must be completed within two weeks of the onset of symptoms, depending on the type of specimen (after which time serum ZIKV RNA levels are too low to be detected),[2] while detecting ZIKV antibodies is challenging due to cross reactivity with other related flaviviruses, leading to false positive results.[3] The limitations of available diagnostic techniques offered an opportunity to develop and bring new diagnostic solutions for use in resource-limited settings, thereby filling a gap in the market.

Intended innovation outcomes

With the growing potential impacts of ZIKV infection and the unavailability of commercially validated in vitro diagnostic tests (IVDs), the SD identified the need for a rapid diagnostic test (RDT) that could be used at the point of care (POC) in programme countries. The rapid ZIKV Dx innovation project is intended to accelerate development and commercial availability of five new diagnostic tools that are accurate (i.e., sensitive and

[1] Sikka, Veronica, et al., 'The Emergency of Zika Virus as a Global Health Security Threat: A Review and a Consensus Statement of the INDUSEM Joint Working Group (JWG)', *Journal of Global Infectious Disease*, vol. 8, no. 1, 2016.
[2] Fourcade, Camille, et al., 'Viral Load Kinetics of Zika Virus in Plasma, Urine and Saliva in a Couple Returning from Martinique, French West Indies', *Journal of Clinical Virology*, vol. 82, September 2016.
[3] Rockstroh, Alexandra, 'Specific Detection of Dengue and Zika Virus Antibodies Using Envelope Proteins with Mutations in the Conserved Fusion Loop', *Emerging Microbes & Infections*, 2017.

specific), rapid and low cost, and that can be used at POC in low-resource settings.

Accurate diagnosis of ZIKV, even without available treatment options, is important to:

- Understand the spread of the disease
- Determine links to other medical conditions (e.g., microcephaly)
- Appropriately identify and manage outbreaks.

The intended use of rapid ZIKV Dx is to diagnose active and previous infection, focusing on pregnant women, and for surveillance purposes. The use of rapid ZIKV Dx in UNICEF programme countries, particularly in Africa, where the environment and presence of the *Aedes aegypti* mosquito are conducive to transmission of the virus, will contribute to surveillance and understanding of the epidemiology of the virus, diagnosis in clinical settings and/or blood banks, and response to future outbreaks of ZIKV.

Innovation users

The target users of rapid ZIKV Dx are health practitioners at POC facilities in low-resource settings. Users in this context may lack access to well-equipped laboratories, and diagnostics will ideally be designed for use by health-care workers with minimal training requirements.

3. CONTEXT FOR DEVELOPMENT OF RAPID ZIKV DX

Key takeaways

- ZIKV was declared a Public Health Emergency of International Concern in February 2016, and there is no specific treatment, vaccine or antiviral therapy available for the virus; available diagnostics require sophisticated procedures that often cannot be completed at POC, creating challenges to diagnosis and surveillance in low-resource settings
- SD identified the limitations of available diagnostic tools to meet programme needs, and responded by communicating to industry the need for an **accurate, rapid and low-cost diagnostic test for use at POC**
- Despite advances in diagnostic capabilities for ZIKV since the outbreak began in 2015, **testing remains limited in low-resource settings**, creating significant delays to receiving test results and making surveillance of ZIKV challenging and expensive; this demonstrates a continued need for affordable and user-friendly diagnostic tests, which the innovation project intends to address.

3.1 Development/humanitarian context

Following the Ebola virus disease crisis in West Africa in 2014, the international community had heightened levels of concern about another epidemic in resource-limited countries. An outbreak of ZIKV in Southern America began with the first case reported in May 2015, following which the Government of Brazil declared a national public health emergency in response to the explosive spread of the virus and coinciding cases of microcephaly, Guillain-Barré syndrome, and miscarriage in pregnant women.[4] As the virus spread across borders, the World Health Organization (WHO) declared a Public Health Emergency of International Concern in February 2016.[5] ZIKV has a mild clinical presentation in which the majority of cases are asymptomatic, and the virus itself lacks a definitive treatment; however, its association with congenital deformities[6] and spread to countries where the

[4] Lowe, Rachel, et al., 'The Zika Virus Epidemic in Brazil: From discovery to future implications', *International Journal of Research and Public Health*, vol. 15, no. 1, 2018.

[5] Heymann, David L., et al., 'Zika Virus and Microcephaly: Why is this situation a PHEIC?', *The Lancet*, vol. 387, no. 10020, 2016.

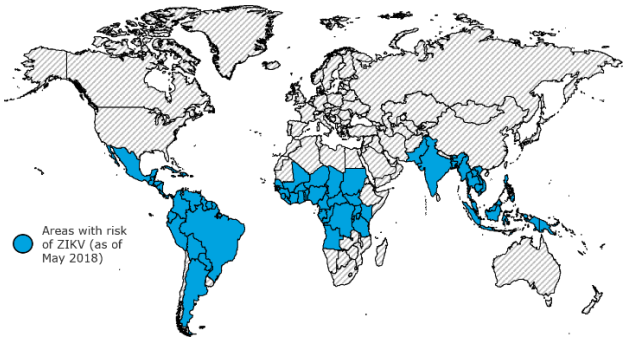
[6] Lowe, 'The Zika Virus Epidemic in Brazil'.

virus was not previously known to be present raised serious international health concerns.

The rapid spread of ZIKV was due to a number of factors, including a large susceptible population, environmental conditions suitable for the mosquito vector, non-vector transmission, and a highly mobile population with ease of travel to and from endemic countries.[7] The single-stranded RNA arbovirus, belonging to the genus *Flavivirus*, is primarily transmitted to humans by the *Aedes aegypti* mosquito. Several cases of sexual transmission of ZIKV from males to females have also been reported, confirmed by the presence of ZIKV RNA in several bodily fluids (e.g., semen, blood, saliva, amniotic fluid, urine) of infected individuals.[8] Other *Flavivirus* to which the spread of ZIKV has been compared include dengue, West Nile and yellow fever virus, in addition to chikungunya virus, a member of the *Alphavirus* family.[9]

As of March 2016, 52 countries and territories had reported transmission of ZIKV to humans, having spread from across the Western Pacific where it was detected in 2007, to the Pacific and the Americas.[10] Currently, several international health authorities (e.g., the United States Centers for Disease Control and Prevention, WHO) are monitoring the transmission of ZIKV, which remains a risk, particularly in low-resource countries in Southern America, West and Central Africa, and the Southeast and Asia-Pacific regions.

Figure 1. Areas with risk of ZIKV, according to the CDC, May 2018[11]



3.2 Innovation context

Based on statistical analysis of the social and economic impacts of ZIKV in Southern America and the Caribbean, there is significant incentive to reduce the burden of disease at the regional level. One study found that spread of the virus between 2015 and 2017 resulted in approximate short-term costs of US$7–18 billion (the lower end of the spectrum being based on 2017 transmission rates, and the upper end of the spectrum on high transmission rates) to the region.[12] Long-term costs are expected to be mainly attributed to the direct and indirect costs associated with microcephaly (estimated lifetime cost of US$8 billion) and Guillain-Barré syndrome (estimated lifetime cost of US$3 billion), both of which have been linked to ZIKV infection. Further, ZIKV is expected to disproportionately impact poor and marginalized populations, due to lower levels of sanitation and infrastructure development that create favourable conditions for the *Aedes aegypti* mosquito, through which ZIKV is spread. The short and long-term finance and human development costs associated with ZIKV demand attention

[7] Imperato, Pascal J., 'The Convergence of a Virus, Mosquitoes, and Human Travel in Globalizing the Zika Epidemic', *Journal of Community Health*, 2016.
[8] Sikka, 'The Emergency of Zika Virus'.
[9] Paixão, Enny S., Maria Gloria Teixeira and Laura C. Rodrigues, 'Zika, Chikungunya and Dengue: The causes and threats of new and re-emerging arboviral diseases', *BMJ Global Health*, 2017.
[10] World Health Organization, 'Emergencies: Zika situation report', 2016.
[11] Centers for Disease Control and Prevention, 'Zika Virus', 2018.
[12] United Nations Development Programme and International Federation of Red Cross and Red Crescent Societies, *A Socio-Economic Impact Assessment of the Zika Virus in Latin America and the Caribbean: With a focus on Brazil, Colombia and Suriname*, UNDP, New York, 2017.

and cost-effective solutions to improve prevention, diagnosis and treatment of the virus.

There is currently no specific treatment, vaccine or antiviral therapy available for ZIKV, and the health response was therefore limited to preventive measures including vector control (*Aedes aegypti* mosquito), prevention of mosquito bites,[13] and use of protective measures (e.g., condoms) during or abstinence from sexual intercourse.[14] Further, diagnosis of ZIKV in infected individuals is a challenge in low-resource settings, as current methods of diagnosis require sophisticated procedures and often cannot be completed at POC. Diagnosis is based on the detection of viral nucleic acid in the relevant specimen by reverse transcription polymerase chain reaction and detection of immunoglobulin antibodies by performing an IgM enzyme-linked immunosorbent assay (IgM-ELISA) followed by a neutralization assay (PRNT) for confirmation).[15] Prior to the ZIKV outbreak in 2015, there were no commercially available diagnostic tests on the market, requiring rapid development of novel products; however, as of 2017, there were 5 serological assays and 14 molecular assays available for use to diagnose of ZIKV infection.[16]

Despite significant advances in diagnostic capabilities for ZIKV, testing remains limited in low-resource settings and specimens are referred from point of collection for testing by trained laboratory technicians in well-equipped laboratories. This creates significant delays to receiving test results and makes surveillance of ZIKV in low- and middle-income countries challenging and expensive. As a result, recent studies of available rapid ZIKV Dx have demonstrated the continued need for affordable and user-friendly POC diagnostic tests appropriate for use in resource-limited countries.[17, 18, 19] Such a diagnostic would increase the efficiency and reduce costs associated with testing, improve in-country diagnostic and surveillance capabilities, and provide infected individuals with timely results for informed decision-making regarding family planning.

3.3 UNICEF programme context

SD, based in Copenhagen, drives external product innovation to prompt and/or accelerate development of fit-for-purpose (i.e., appropriate to achieve the intended results) and value-for-money (i.e., optimal combination of cost, quality and sustainability) products with potential to positively affect UNICEF programmes. The division is able to leverage UNICEF's procurement power and technical expertise to drive PIPs, which are initiated when there is an unmet product need in UNICEF programmes and/or emergency response. In 2017, UNICEF procured approximately US$3.46 billion worth of supplies and services for children in 2017, including US$108.7 million in medical supplies and equipment.[20] PIPs can apply to products that do not exist or are not in procurable form. While the rapid ZIKV Dx project did not begin as a standard PIP, it followed a similar process. SD accelerates development of product innovations that encourage healthy markets and diversify the supplier base, complementing UNICEF's unique position to understand global needs for new or improved product offerings, convene stakeholders, and drive scale.

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[13] World Health Organization, 'Vector Control Operations Framework for Zika Virus', 2016.
[14] World Health Organization, 'Prevention of Sexual Transmission of Zika Virus', 2016.
[15] United States Centers for Disease Control and Prevention, 'Diagnostic Tests for Zika Virus', 2018.
[16] Theel, E. S. and J. Hata, 'Diagnostic Testing for Zika Virus: A postoutbreak update', *Journal of Clinical Microbiology*, vol. 56, no. 4, 2018.
[17] Ibid.
[18] Chura, A., et al., 'Update on Zika Diagnostic Tests and WHO's Related Activities', *PLOS Neglected Tropical Diseases*, vol. 11, no. 2, 2017.
[19] Wand, N., et al., 'Point-of-Care Diagnostic Assay for the Detection of Zika Virus Using the Recombinase Polymerase Amplification Method', *Journal of General Virology*, vol. 99, 2018.
[20] United Nations Children's Fund, *Supply Annual Report 2017*, UNICEF Supply Division, Copenhagen, 2018.

According to SD, product innovation projects should:

- Be **fit for purpose**
- Provide **value for money**, including better pricing for use in low-resource settings
- Drive **research and development, availability and scale**

When the ZIKV outbreak began to spread across Southern American countries, the Pan American Health Organization (PAHO), WHO and SD identified the limitations of current diagnostic techniques to meet programmatic needs. Recognizing these challenges, SD and its partners determined that they would communicate the need for an accurate (i.e., sensitive and specific), rapid and low-cost diagnostic to industry. SD decided to communicate a set of required and ideal product characteristics to guide industry towards a diagnostic for use in resource-limited countries. To incentivize investment in R&D of rapid ZIKV Dx, USAID provided funding to establish an Advance Purchase Commitment (APC) to guarantee procurement of a certain quantity of product, de-risking product development. The rapid ZIKV Dx project marked the first use of APCs for both SD and USAID, offering opportunities for learning about not only the process of product innovation, but also the use of alternative financing mechanisms.

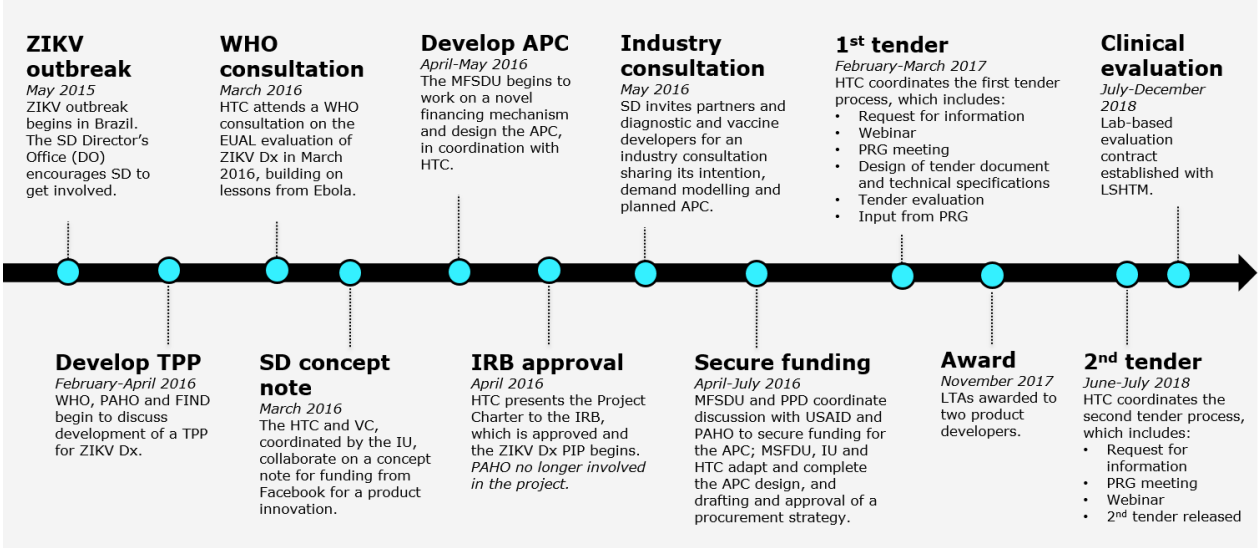
4. THE INNOVATION JOURNEY FOR ZIKA DX

Key takeaways

- After identifying the need for research and development (R&D) of a rapid diagnostic test that could be administered at point of care, SD, WHO, PAHO and FIND developed a **TPP to drive development of products** that are fit-for-purpose in low-resource settings
- USAID joined as a partner, providing a **grant of US$10 million** to offer a **pull mechanism to developers and manufacturers through an APC**, reducing the risk associated with investment in R&D for new diagnostic products; following the first tender process, two manufacturers were selected for LTAs including APCs
- **Consultation during design of rapid ZIKV Dx was substantial**, involving participation of SD, industry, academia and partner organizations, and played an important role in shaping and validating certain components, such as the demand forecast
- **Regulatory approval has been a challenge** during the project, and **an iterative approach has enabled SD to adapt accordingly**, for example, by contracting LSHTM to complete clinical evaluations and removing Emergency Use Assessment and Listing procedures from regulatory approval requirements
- While the first tender did not specify a preference for a singleplex or multiplex diagnostic tool, the focus of the second tender on multiplex diagnostics will **provide a comparative market advantage** in terms of surveillance capabilities and the continued relevance of products.

The innovation pathway for rapid ZIKV Dx (Figure 2) follows the stage-gated process developed by SD for PIPs. The innovation process is not yet complete, as products selected for LTAs and APCs in the first round have yet to complete clinical evaluation, an important step towards achieving the regulatory approval required to move to commercial availability. Further, in June 2018, SD and its partners launched the second tender, which will select manufacturers for LTAs and APCs, focusing on development of multiplex diagnostics that can differentiate between different viral infections.

Figure 2. Innovation pathway for rapid ZIKV Dx, as of October 2018



Needs identification

Identification of the need for POC ZIKV diagnostics

Following WHO's declaration of the ZIKV outbreak in Southern America as a public health emergency, USAID issued a Grand Challenge for Development of US$30M to combat ZIKV and future threats of infectious disease.[21] The challenge focused on innovations in preventive measures (e.g., vector control and household protection), detection, surveillance and community engagement. As one of the major procurers of diagnostics and a large procurer of vaccines, SD had a particular interest in the type of product development that could contribute to these measures, and decided to explore the need for vaccines and diagnostic tools.

Recognizing the challenges described in Section 3.2, the key issues resulting from limited capacity to diagnose individuals infected with ZIKV at POC are twofold:

- Reduced chances to **inform infected individuals of the risks** associated with ZIKV (e.g., risk of fetus developing microcephaly due to infection of pregnant women). This diminishes the ability of infected individuals to make informed choices regarding birth control, termination of pregnancy, and monitoring the development of the fetus with microcephaly throughout pregnancy.
- Developing a better **understanding of the epidemiology** of ZIKV, its presence and levels in populations, and its links to other health conditions (e.g., Guillain-Barré syndrome) is more difficult due to poor surveillance capabilities.

In addition to the issues identified above, challenges and the needs of product developers related to research, development and deployment of diagnostics were identified. In the case of diagnostics for use in resource-limited contexts, barriers found to delay product development and market availability include insufficient prioritization, difficulty attracting investment, complex regulatory environments, and quality assurance.[22] For rapid ZIKV Dx, there was

[21] United States Agency for International Development, 'Combating Zika and Future Threats: A grand challenge for development', USAID, 2018.

[22] The Academy of Medical Sciences, 2016. 'Improving the Development and Deployment of Rapid Diagnostic Tests in LMICs', Workshop Report, 2016.

potential to accelerate market availability of novel products by specifying the criteria (e.g., regulatory approval) required for procurement, while ensuring that there were processes in place for product developers to meet those requirements (e.g., clinical testing of new products provided through a contractor) and sufficient incentive for product development. This would enable SD and its partners (WHO and PAHO, which were involved in the development of the TPP) to better meet the needs of product developers.

Recognition and exploration

Development of the Target Product Profile

Development of the Target Product Profile (TPP) for Zika Dx was an important aspect of accelerating development of diagnostics that were fit-for-purpose and cost-effective for use in programme countries (i.e., countries in which UNICEF delivers programmes) and/or low-resource settings (i.e., environments with minimal health infrastructure). TPPs are a tool commonly used to drive R&D of pharmaceuticals and diagnostics. SD uses TPPs to communicate requirements to developers and manufacturers, for products that do not exist, but would fulfil a need for UNICEF and its partners.[23] TPPs communicate requirements on the purpose of a new (or improved) product, including the minimum and ideal performance criteria.

PAHO, FIND and WHO began to develop a TPP for ZIKV Dx in April 2016, keeping criteria broad, as at the time the partners did not know exactly what specifications would be ideal for development of diagnostic tools specific to ZIKV. Following encouragement from the SD Director's Office to become involved in the response to the ZIKV outbreak, SD approached the group developing the TPP, offering to contribute and to make it a joint initiative; this was the first joint TPP in which UNICEF was involved. During TPP development, partners provided guidance on prioritization of needs for ZIKV Dx, offering expertise on surveillance, research and patient needs. Further, WHO develops an annual Blueprint list of priority diseases based on public health risks associated with diseases for which there are no, or limited, countermeasures.[24] Development of the Blueprint strategy for ZIKV (included on the priority list) included a rapid landscaping effort and consultation with academics, manufacturers and regulators on R&D and future priorities. The road map developed yielded important information regarding current and future needs to respond to the ZIKV epidemic, and was an important input for development of the TPP.

The TPP included both single and multiplex diagnostic tools (Table 1), which will contribute to diagnosis and surveillance of ZIKV, respectively.

Table 1. Definitions of single and multiplex diagnostics for Zika and other arboviruses

	Singleplex	Multiplex
Purpose of diagnostic[25]	Used to detect one target sequence of DNA or RNA.	Used to detect two or more target sequences of DNA or RNA simultaneously.
Intended use for rapid ZIKV Dx	Diagnostic intended to diagnose previous or active infections of ZIKV.	Diagnostic intended to provide differential diagnosis of previous or active infection, able to distinguish between ZIKV, yellow fever, chikungunya and dengue virus.
Purpose of testing	Diagnosis of ZIKV, particularly for pregnant women, family planning and blood bank testing.	Diagnosis of different viral infections, particularly for antenatal clinics, blood bank testing, and surveillance.

[23] United Nations Children's Fund, 'Target Product Profiles', Supply Division, 2018.
[24] World Health Organization, *2018 Annual Review of Diseases Prioritized under the Research and Development Blueprint*, WHO Research and Development Blueprint, 2018.
[25] LabCE, 'Singleplex versus Multiplex Assay', 2019.

Prior to finalizing the TPP, WHO hosted a meeting from 7 to 9 March 2016 to plan the accelerated development and evaluation of products (including diagnostics and vaccines) to respond to the ZIKV outbreak. As convenor, WHO brought together a variety of stakeholder groups that could contribute to the response, including virology experts, clinicians, product developers, funders and development partners.[26] The Health Technology Centre (HTC) attended the conference on behalf of SD.

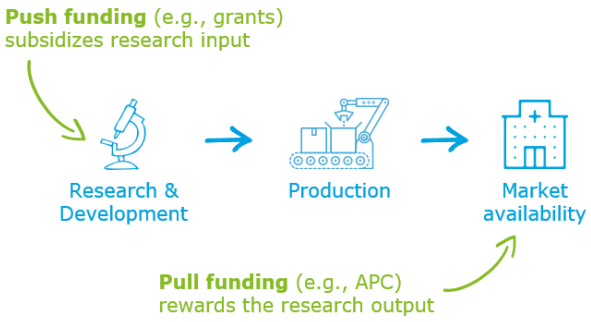
Following development of the TPP, the HTC, Vaccine Centre and IU started regular discussions to come up with a project focused on rapid diagnostics to respond to ZIKV. Development of the project idea was a collaborative process, with consideration of technical specifications, contracting and financing. The team drafted a concept note for funding from Facebook for diagnostic and vaccine product innovations, and ultimately decided to approach USAID for funding.

Development of Advance Purchase Commitments to de-risk investment in R&D

SD, in close collaboration with a supportive donor, decided to utilize a pull mechanism (Figure 3) to incentivize product development. The Markets, Finance and Strategic Data Unit (MFSDU), in coordination with HTC, designed an APC to accelerate and de-risk R&D of rapid ZIKV Dx and reduce barriers to manufacturers' entry to the market. APCs are a form of contracting through which a procurer guarantees that it will purchase awarded volumes from the manufacturer, regardless of the materialization of demand.

The design of the mechanism was such that SD would award manufacturers LTAs for procurement over a period of three years, including a guaranteed off-take for a portion of the forecasted amount of product to be procured. Importantly, the guarantee was contingent upon the product meeting certain criteria in terms of regulatory approval and performance and subject to SD's evaluation of the actual appropriateness of the product.

Figure 3. Push funding vs. pull funding.
An Advance Purchase Commitment is a type of pull mechanism used to incentivize profit-seeking investments, for example into R&D to develop a rapid ZIKV Dx. APCs encourage investments through a guarantee of the purchase of pre-specified quantities at a negotiated price for products that meet a set of predetermined specifications.



Using demand forecasts to communicate need

In order to demonstrate the need and potential market for rapid ZIKV Dx to manufacturers, SD developed a potential demand forecast model built on the assumption of the needs that would materialize. The demand forecast model was based on countries at risk of outbreak due to presence of the *Aedes aegypti* mosquito and environmental transmission suitability since the international community did not have a good understanding of ZIKV epidemiology at the time. The model included the 20 countries likely to channel procurement through SD (about 80 per cent of total forecasted demand) and excluded countries in Southern America (since ZIKV Dx were to be procured through PAHO, not UNICEF, for this region at the time the forecast was developed), China, India and Indonesia. The assumption for the number of tests required was that 35 per cent of the

[26] World Health Organization, *WHO Global Consultation on Research Related to Zika Virus Infection*, R&D Blueprint, 2016.

primary target cohort (pregnant women and their male sexual partners) would be tested annually, based on antenatal coverage rates observed for an HIV RDT. Also included in the forecast were clinically diagnosed cases of microcephaly (assuming 1 per cent of the primary cohort), GBS (assuming 0.5 per cent of the primary cohort) and travellers to and from areas with ongoing ZIKV transmission (assuming 0.5 per cent of the primary cohort).[27] The total forecasted demand for RDT/POC tests was approximately 40 million from 2017 to 2019. Understanding the potential demand for diagnostics allows product developers and manufacturers to better understand the market and potential return on investment in R&D.

Consultation with industry

In May 2016, SD hosted a two-day industry consultation in Copenhagen, focused on ZIKV Dx and vaccines. Attendees of the supplier conference included partners, and diagnostics and vaccine manufacturers with the potential to develop viable products and advance the commercial environment to address challenges related to ZIKV. Fifty-two individuals (external to SD) attended the two-day consultation that included presentations on demand, SD's procurement approach, and product requirements. Several partners presented at the conference, including an overview of the regulatory pathway for ZIKV Dx by WHO and the US FDA. At the time of the industry consultation, SD was in discussions with USAID (also in attendance) to secure committed funding for the APC.

During the industry consultation, TPP and APC considerations for ZIKV Dx were presented. Feedback was gathered prior to the industry conference through a public consultation hosted on the WHO website from March to April 2016. The need/demand-forecasting model was also presented at the supplier conference, during which SD received constructive feedback on its model and assumptions prior to moving forward with the project. Of the potential demand for rapid ZIKV Dx forecasted, SD presented a potential purchase commitment of about 15 million RDTs and/or 6 million POC tests over three years (2017–2019), up to a value of US$10 million. Upon reviewing this information, developers and manufacturers indicated that the desired cost per unit was too low. In response, the first tender process included firm commitments for procurement of up to the following number of tests through the APC:

Table 2. Amounts up to which SD would consider procuring through APCs in the first tender

DIAGNOSTIC TYPE	NUMBER OF TESTS UP TO WHICH SD WILL PROCURE
Serological and molecular IVDs using an RDT platform (single or multiplex format)	4 million
Serological and molecular IVDs using RDT and POC platforms (single or multiplex format)	4 million
Serological and molecular IVDs using RDT and POC format (multiplex format only)	7 million

During the industry consultation, the exact cost per unit that SD was willing to pay was not presented. However, the amount available in the form of an APC and the number of tests to be procured through the APC provided developers and manufacturers with an idea of the target price for individual tests. Included in the conditions of the LTA was that the cost of non-APC procurement must be less than or equal to the cost provided for APC procurement.

The industry consultation process for ZIKV Dx provided manufacturers and academia the opportunity to offer feedback and shape development of the APC and RFP for the product innovation. Alignment on each of these documents was crucial in order to generate buy-in from industry to develop ZIKV Dx suited to the needs of SD and its partners for use in programme countries. The consultations also allowed SD to test and validate its

[27] United Nations Children's Fund, 'Request for Proposal: Zika Virus (ZIKV) Diagnostics (for Testing at Point-Care) Including for Access to an Advance Purchase Commitment (APC)', RFP-DAN-2017-502425, 2017.

assumptions on rapid ZIKV Dx (e.g., potential demand forecasts, target unit price) and integrate expertise and learnings from a greater variety of stakeholders, strengthening the overall innovation process.

In addition to the industry consultation, SD completed product mapping to determine the status of products that were or would be in development. This was based on a Request for Information from UNICEF's diagnostic supplier database, and analysis of the product pipeline for ZIKV products (i.e., diagnostics, vaccines, therapy) completed by WHO, which included mapping of manufacturers considering or actively developing ZIKV Dx. Further landscape analysis was completed through direct consultation with manufacturers focused on RDTs. Product mapping helped SD and its partners to generate a better understanding of how close rapid ZIKV Dx were to being market-ready.

APC funding and approval as a PIP

Following the industry consultation and finalizing the APC design, SD secured a US$10 million grant from USAID to fund the APC. The USAID Center for Accelerating Innovation and Impact partnered with SD to create the APC (the first of its kind for USAID and UNICEF) as part of the response of the organization to the ZIKV epidemic. The Center takes a market-based approach to innovation, using non-traditional financing tools to promote business-minded approaches to addressing gaps and bottlenecks to development. This complements the approach to product innovation taken by SD.

After securing the funding required to execute the APC, the HTC presented the Project Charter to the IRB. Shortly after approval of the project by the IRB, PAHO (originally intended to procure diagnostics for use in Southern America, in which demand for rapid ZIKV Dx is greatest) came to the internal decision that it would no longer continue with the project as a partner. There seems to be a general lack of alignment on the exact circumstances that led to PAHO's departure from the project, and its level of contribution to the project while involved. However, based on interview responses it appears to be mainly due to differences of opinion in terms of approach to the ZIKV response, as PAHO did not view itself as a player in the market-influencing space (one partner); and the organization questioned the need for an APC and whether preference should be given to multiplex over singleplex diagnostics (three SD).

The **Innovation Review Board** (IRB) is the decision-making body for SD PIPs, responsible for deciding whether a product should advance to the next stage of the innovation process, including whether funding should be allocated from the US$500,000/year innovation budget or from project-specific donors, remain in the same stage, or be closed. The Project Team presents project updates to the IRB at key points in the life cycle of the innovation – for example, to obtain resources for field-testing, or to receive input on significant decisions.

Development and implementation

Following approval of rapid ZIKV Dx as a PIP, the HTC and MFSDU coordinated the operation side of the project, to complete drafting the procurement strategy and start preparation of the first tender process. This included developer and manufacturer engagement, and preparing the RFP.

Design of the RFP and technical specifications

An important aspect of the RFP design was consideration of the complex regulatory environment for diagnostics, which differs between regions and countries in which the products may be used. Accordingly, regulatory approval was a condition for LTAs to be awarded to successful applicants. The required regulatory approvals included in the RFP were:

- WHO Pre-qualification for Medicinal Products
- WHO Emergency Use Assessment and Listing (EUAL) or US FDA Emergency Use Authorizations (EUA)
- Stringent Regulatory Authority (SRA) approval
- ISO 13485:2003 Medical Devices – Quality management systems – Requirements for regulatory purposes.

Both WHO and US FDA were essential partners for determining regulatory approval requirements for products, as detailed in the first tender through their expedited regulatory review processes. Having recently responded to another outbreak of global health concern, Ebola virus, the organization brought valuable expertise on the development of diagnostics for emergency response. For example, in response to the variability of quality and performance of diagnostics supplied during the Ebola outbreak, WHO established the Emergency Use Assessment and Listing (EUAL) Procedure that is activated upon declaration of a Public Health Emergency of International Concern, to list products based on minimal evidence of safety and efficacy. In July 2015, WHO established an EUAL and published the submission criteria for IVDs for ZIKV nucleic acid testing and serology IVD, intended to provide guidance on the quality, safety and performance of diagnostics following independent assessment based on the outcome of their consultation early March.[28] US FDA has a similar mechanism, Emergency Use Authorization (EUA).

The Quality Assurance (QA) Policy for the Procurement of Rapid Diagnostics/POC Technology (developed by the SD Quality Assurance Centre and HTC) describes the regulatory and quality standards for the selection and procurement of rapid ZIKV Dx.[29] The QA policy was developed for this innovation as SD and its partners are accelerating market availability and access to diagnostics that may have yet to undergo standard regulatory evaluations. The policy was intended to bridge this gap by requiring that a minimum level of vigilance be applied to products offered. SD QA standards for IVD products, such as rapid ZIKV Dx, require that products be manufactured under a Quality Management System (QMS), using the standard *ISO 13485:2003 Medical Devices – Quality management systems – Requirements for regulatory purposes* as a benchmark. In addition to the application of QMS to all sites and locations used to manufacture diagnostics, in order to meet the QA requirements for procurement by SD, ZIKV Dx must also meet the criteria listed in the table below.

Table 3. Requirements for SD procurement of ZIKV Dx

REQUIREMENT	DESCRIPTION OF THE MECHANISM
The product must obtain WHO prequalification	The WHO List of Prequalified Medicinal Products includes products for which data submitted by the manufacture supplier have been evaluated, WHO have inspected relevant sites, and requirements for WHO prequalification are met. The list is used by United Nations organizations for evidence-based selection of products and procurement from manufacturing sites included on the list.
The product must undergo either WHO EUAL or US FDA EUA	The EUAL Procedure applies to IVDs in health situations declared a Public Health Emergency of International Concern. The listing provides United Nations procurement agencies and National Regulatory Authorities with information on the quality, safety and performance of IVDs. EUAL procedures include a review of technical and QMS documentation, and an independent laboratory evaluation for product performance. The US FDA EUA legal procedure is used to approve new health products for use during public health emergencies for which there are no adequate, approved or available alternatives.
The product must be approved by an SRA	A Stringent Regulatory Authority (SRA) designated by one of the five founding members of the Global Harmonization Task Force Competent Authorities can approve use of finished products. The task force is an international group that includes medical device regulatory authorities and trade associations from the European Union, the United States, Canada, Japan and Australia.

[28] World Health Organization, 'WHO Emergency Use Assessment and Listing (EUAL) Procedure', 2016.

[29] United Nations Children's Fund, 'Quality Assurance Policy for the Procurement of Rapid Diagnostics/Point of Care Technology', UNICEF Supply Division Quality Assurance Centres and Health Technology Centre, 2016.

Approval by the above regulatory bodies will minimize the risk of bottlenecks due to varying national regulatory environments for health-care products. In the second tender, the requirement for WHO EUAL or US FDA EUA was removed, as following the declaration of the end of the ZIKV Public Health Emergency of International Concern, product applications (already applied or new) will not be assessed under EUAL procedures.

Launch of the first tender

SD launched the first RFPs in February 2017. The objective of both tenders was to establish LTAs with, and potentially award APCs to, developers and manufacturers to accelerate the supply and market availability of two novel and affordable ZIKV Dx products through SD for 2017–2019. This was part of a larger goal to create a healthier and more competitive market for ZIKV Dx. The types of diagnostics covered included RDT Antibody (Ab) detection, RDT Antigen (Ag) detection, and POC nucleic acid testing technology.

Selection of developers and manufacturers for LTAs

The process for evaluating proposals submitted to SD follows United Nations procurement protocols. The criteria for selection and evaluation methodology must be clearly specified in the RFP. SD completes a technical evaluation first, followed by a commercial evaluation.

- **Technical evaluation:** SD completes a review of the mandatory technical requirements detailed in the RFP. Products that meet these criteria are then evaluated against remaining technical criteria
- **Commercial evaluation:** SD evaluates proposals according to their quantitative and qualitative content (e.g., affordability, production capacity, quality), in line with the Procurement Strategy.

SD and USAID highlighted the preference for multiplex diagnostics during the tender process, to which the Procurement Reference Group (PRG; group of technical experts that provides direction and support to the Project Team) agreed. This decision, coupled with agreed-upon prices ensuring affordability, should improve the likelihood for success and sustainability of rapid ZIKV Dx. Developing diagnostics that can detect multiple types of viral infection will theoretically protect products from significant changes in demand resulting from fluctuations in interest in diagnosis and surveillance of arboviral diseases over time. Thus, stable and affordable prices and the ability to diagnose different arboviruses should support creation of a sustainable and reliable market for multiplex diagnostics.

The RFP for rapid ZIKV Dx also considered the capacity of developers and manufacturers to provide an uninterrupted, sustainable supply of product. During the evaluation and selection of proposals in the first tender, quantitative and qualitative criteria were considered, including lead time, monthly production capacity, and the manufacturers' experience in diagnostic production and performance records.

The first tender received responses from six developers and manufacturers, from which SD, with guidance from subject matter experts in the PRG, selected two products for which SD awarded developers 36-month LTAs. In order to compare proposed products, the rapid ZIKV Dx Project Team first evaluated proposals according to the minimum acceptable criteria, eliminating those that did not meet the specifications detailed in the RFP. The Project Team then used a points system to compare products, awarding points based on certain suggested characteristics, including the sensitivity and specificity offered, and whether the product was a single or multiplex diagnostic. However, despite applying this approach to compare products, it could not offer differential evaluation because each product had different strengths and weaknesses, resulting in an 'average score' for each proposal. Therefore, the team evaluating proposals used the general requirements, through which SD was able to prioritize proposals.

In December 2017, SD awarded Conditional LTAs to Chembio Diagnostics Systems Inc. and SD Biosensor for rapid ZIKV Dx, with access to an APC subject to meeting the conditions of the offer. Both manufacturers selected for LTAs had an existing relationship with SD (e.g., SD

procures glucosamine through SD Biosensor and HIV test kits from Chembio) prior to being invited to participate in the industry consultation. The product developed by Chembio Diagnostics Systems Inc. is a singleplex ZIKV IVD assay, while the product developed by SD Biosensor is a multiplex IVD assay for detection of ZIKV, dengue and chikungunya viruses. Through the process of technical evaluation, it was highlighted that developers had faced challenges to obtain a well-characterized serum panel to validate their assays; this was due to limited availability of serological samples of ZIKV, and that available commercial panels were not validated by regulatory authorities. In response to this challenge, SD contracted LSHTM to complete clinical evaluations by designing a panel and conducting lab-based validations, which, as of September 2018, is in progress for products selected, and which SD expects to be complete in the fourth quarter of 2018.

Development and launch of the second tender

Despite delays to market availability of the products selected for LTAs through the first tender process, SD released the second tender in June 2018, and expects to issue second-round contract awards in the fourth quarter of 2018. Development of the second tender followed a similar process to the first, beginning with a Request for Information, followed by a meeting of the PRG. SD hosted an industry webinar in May 2018 for interested developers and manufacturers, to provide an update on project developments, outcomes of the first tender, clinical evaluation status, demand profiles, and SD's procurement approach and timelines for the second tender.

Since issuing the first tender, SD/HTC has gained greater insight to the diagnostic products, markets and development processes, reflected in updated SD technical requirements focused on multiplex assays and procurement volumes in the second RFP.

Table 4. Amounts up to which SD would consider procuring through APCs in the second tender

DIAGNOSTIC TYPE	NUMBER OF TESTS UP TO WHICH SD WILL PROCURE
Serological and molecular IVDs using RDT and POC platforms (multiplex format only)	2 million
Serological and molecular IVDs using RDT and POC platforms (singleplex format only)	0.5 million

The objective of the second tender is to establish LTAs for the supply of rapid ZIKV Dx, with US$7 million remaining for APCs (based on the US$1.5 million in conditional firm commitments awarded for procurement of product from each of the two manufacturers selected in the first tender process). Although there is an increased number of rapid ZIKV Dx available on the market, recent market analysis has shown a continued gap in diagnostic tests intended for use in resource-limited countries and for POC testing, which supports SD and project partners' decision to proceed with the second tender. Further, while the first tender did not specify preference for one type of diagnostic tool, the focus of the second tender is the sustained supply of multiplex diagnostics, which will allow for differential diagnosis among related arboviruses. Multiplex diagnostics will allow for simultaneous detection of ZIKV, dengue, chikungunya and yellow fever virus. This will provide a comparative market advantage in terms of surveillance capabilities, as well as continued relevance of products developed in the case that ZIKV becomes less of a global priority.

Outlook for ZIKV Dx

The outlook for ZIKV Dx is still relatively unknown, as:

- Developers and manufacturers awarded LTAs have not yet started delivery of products and must first meet regulatory requirements
- The results of the second tender will likely be more indicative of whether the APC has facilitated development of new diagnostic tools that would otherwise have not been developed
- Demand assumptions cannot be verified unless there is another outbreak of ZIKV.

The next steps for SD to accelerate access to rapid ZIKV Dx will be to begin to support Programme Division (PD) in creating demand in target countries. This may present a new set of challenges for the product innovation. In previous discussions with the UNICEF Regional Office for Latin America and the Caribbean (LACRO) regarding the UNICEF ZIKV Regional Strategy for 2018-2019, SD recommended adding the creation of demand and piloting of RDT ZIKV Point-of-Care Diagnostics under the activity "1.4. Detection and surveillance contribute to early diagnosis in pregnant women and surveillance". Utilizing UNICEF programmes on the ground, LACRO would not need to pay for freight and tubes for samples; however, despite its addition to the strategy, low interest at the regional level persists. In order move rapid ZIKV Dx toward scale, SD will need to begin to generate interest and political will for use of the products regionally and in country.

MINILOAD 2
LONG LINE

5. FINDINGS

5.1 Approach dimension

1. How does this innovation contribute to UNICEF country and global strategies?

This innovation contributes to **UNICEF's response to ZIKV**, which includes a global plan to monitor, assess and respond to the likely continued spread of the virus across regions.[30] This is aligned with the **inter-agency WHO Zika Strategic Response Plan**, of which UNICEF is party, which guides the international response to ZIKV, including prevention, detection, care and support, research and coordination.[31] Rapid ZIKV Dx development supports UNICEF's programme target to accelerate development and availability of at least two diagnostic tests, to improve identification, understanding and surveillance of the virus.

2. What is this innovation doing in terms of scaling up and out or working at greater efficiency and economy?

This innovation is about doing something new, scaling up, and working at greater efficiency/economy:

- **Doing something new:** The rapid ZIKV Dx project will drive development and market availability of novel diagnostic products that can be administered at POC. SD identified the need for development of a rapid test, which does not currently exist in the market.
- **Scaling up:** In the rapid ZIKV Dx Procurement Strategy, SD describes that scale-up of novel products will be achieved through integration of diagnostics into countries' testing algorithms. SD will support the Programme Division to work with governments, Country Offices (COs) and Regional Offices outside of the Latin America and the Caribbean Regional Office (LACRO) to develop prevention and response plans for ZIKV that include procurement of diagnostics.

Working at greater efficiency/economy: In addition to consideration for a low-cost diagnostic to improve the affordability of novel products, the tender process is designed to accelerate development of multiplex diagnostics that will apply to more than ZIKV and will likely improve longevity and usefulness of the diagnostic. The multiplex diagnostic(s) will allow health care practitioners to distinguish between ZIKV, dengue, chikungunya and yellow fever virus infections. While there is no specific treatment for arbovirus infection, differential diagnosis of arbovirus will improve the surveillance capabilities of the international health community in healthy and unhealthy populations, leading to improved understanding of the virus. The application to other viruses is also advantageous, as the diagnostic will remain relevant regardless of level of concern regarding ZIKV.

3. How are end-user needs identified and considered and how did they shape the innovation?

The needs of end users of ZIKV Dx were considered through **development of acceptable and ideal characteristics of novel diagnostics in the TPP(s)**. The diagnostics procured by SD through developers and manufacturers holding LTAs are intended for use by health-care practitioners in low-resource settings at POC. Design of the TPP included considerations for the unique challenges created by use of diagnostic tools by individuals with minimal training in regions that lack access to well-equipped laboratories. Based on feedback from a manufacturer awarded an LTA during the first tender process, the minimum acceptable and ideal requirements described in the TPP were successfully utilized to guide product development. For example, the TPP motivated one manufacturer to improve sensitivity and specificity, ensure that its diagnostic was easy to use, and provide user-friendly training materials utilizing images rather than text.

[30] United Nations Children's Fund, 'Zika Response', 2016.

[31] World Health Organization, 'Zika Strategic Response Plan: Revised for July 2016–December 2017', 2016.

Although diagnostics selected in the first tender process were already in development prior to launching the RFP, manufacturers were able to refine product design and ensure that products were user friendly for users with limited access to training and/or sophisticated technical equipment.

4. What challenges were faced during the innovation process and what strategies were used to overcome barriers?

The Project Team faced several challenges over the course of the innovation process, including:

- The **rapid response may have left gaps in understanding of market enablers and constraints** faced by industry. Several stakeholders in the innovation process expressed that there was not enough time to complete a deep dive into the economics of rapid ZIKV Dx development to understand the market barriers and challenges faced by developers and manufacturers. This missing piece may have helped strengthen and tailor design of the pull mechanism to improve future outcomes.

- **Regulatory challenges** have arisen due to the complexity of dealing with requirements for diverse products and identifying appropriate regulatory frameworks (one SD, two IRB),[32] and creating the reference panels due to limited availability of serological samples for clinicial evaluations. For example, SD requires that products receive approval from a Stringent Regulatorty Authority prior to procurement; however, manufacturers have requested that Conformité Européene (CE) marking be accepted (one SD). CE marking is self-certified by the manufacturer, which was identified as a risk and not compliant with the SD Quality Assurance Policy for the Procurement of Rapid Diagnostics/POC Technology, and so the request was denied. Regulatory approval requirements were also a challenge with PAHO, as UNICEF could not accept approval from Brazil ANVISA (*Agência Nacional de Vigilância Sanitária*) as it is not a United Nations-approved SRA (two SD). This created additional challenges to the partner relationship with PAHO.

- Regulatory approval delays due to challenges related to clinical evaluation could **reduce the benefits of an LTA and APC** for manufacturers selected through the first tender process, as LTAs are already in effect and expire within three years of signing, after which time SD is no longer obligated to procure product. Although manufacturers are pleased with the decision to move forward with LSHTM for lab-based validation (two manufacturers), such delays could reduce interest in future PIPs using similar pull mechanisms.

- SD and PAHO had **challenges from a partnership perspective** due to differences of preferred approach to ZIKV response (e.g., preference for a singleplex or multiplex diagnostic) and differences in time frame to respond to the crisis. PAHO needed to prioritize responding to the crisis on the ground, while SD was focused on the availability of fit-for-purpose supplies and therefore driving production innovation, despite the long period required (*see question 23 for details*).

5. How was scale considered through the process, starting with the initial design of this innovation?

Because the rapid ZIKV Dx PIP was in response to a public health emergency, planning for scale was difficult, as it takes several years for products to move to commercial availability, and there was pressure to begin the process and accelerate R&D. While issues of ownership and scaling were considered, it was difficult to fully scope out the plan for scale while the emergency was still evolving. However,

[32] Content in parentheses in the findings section indicates the number of interviewees by stakeholder group that expressed the stated idea.

development of the RFP included considerations for scale-up of diagnostics from a market perspective.

Commercial evaluation of diagnostics submitted in response to the first tender included considerations for affordability of quality products and ability of manufacturers to meet global procurement demands.[33] Preference was given to products with the shortest time to development and lowest acceptable prices, in order to reduce the time needed to move products selected to commercial availability and improve the cost-effectiveness of diagnostics to facilitate implementation and scale-up. For example, one of the tender objectives listed in the RFP was reliable, uninterrupted supply of product, which was evaluated according to criteria including lead time, monthly production capacity, and proven capacity to supply offered and forecasted quantities. Criteria such as these were crucial to ensure that manufacturers offered LTAs that would meet demands for affordable diagnostic products.

> *Insights*: Several interviewees (one SD, two IRB) expressed concern regarding future demand for rapid ZIKV Dx, and what SD's role should be in supporting the Programme Division to **generate demand**. If clinical evaluations demonstrate that the product works, and SD moves to procurement of rapid ZIKV Dx to fulfil APCs, the project could face several issues, including lack of demand and/or early adoption of innovative products.

6. Was a proof of concept and business case developed for this innovation?

SD developed **a potential demand forecast to demonstrate the need and potential for procurement** to product developers and manufacturers, based on countries at risk of ZIKV outbreak due to the presence of the *Aedes aegypti* mosquito and environmental conditions. Based on interviewee feedback (three SD, one IRB), developing the demand forecast was challenging due to limited understanding of the epidemiology at the time. As response to the ZIKV outbreak was a time-pressured effort, the model was based on that of dengue, a related arbovirus transmitted by the same vector, and was presented for input from technical experts at the industry consultation hosted by SD. One manufacturer that was awarded an LTA through the first tender process noted that while their product was already under development prior to the industry consultation, the demand forecast and conference provided an entry point for engagement with UNICEF.

7. How does this innovation complement or build on existing knowledge and work conducted in the country and across programmes?

Existing work being conducted at the developer and manufacturer level influenced the innovation process. Product mapping, analysis of the diagnostic landscape and industry consultation helped to test project partners' assumptions and to refine the innovation strategy. In the exploration phase of the PIP, SD and its partners understood that development of a differential diagnostic tool (i.e., multiplex) was not as close as a singleplex diagnostic, due to increased complexity and time required for R&D. Accordingly, the first tender focused on accelerating development of either a singleplex or multiplex diagnostic, while the focus of the second tender favours a multiplex diagnostic. This approach intends to enable SD and its partners to optimize time to market, through a two-phased strategy focused short- and long-term product development.

8. How have the local environment/market (including legal, regulatory and technological) considerations influenced the design of the innovation?

Since rapid ZIKV Dx are intended to be used across programme countries at risk of spread of the virus, it was important to **consider regulatory requirements in the design of the innovation, in order to be appropriate for**

[33] United Nations Children's Fund, Request for Proposal: Zika Virus (ZIKV) Diagnostics (for Testing at Point-of-care), Including for Access to an Advance Purchase Commitment (APC), RFP-DAN-2017-502425, 2017.

supply. Regulatory requirements for ZIKV Dx demand that manufacturers receive approval by an SRA, including the new In Vitro Diagnostic Regulation in the European Union, within five years. Although the regulatory approval requirements, developed in consultation with WHO, were necessary to ensure the quality of new diagnostic products procured through SD, the approval process has delayed progress towards market availability of products selected for LTAs during the first tender.

9. What value does UNICEF bring to this innovation and what makes UNICEF suitable to scale it?

UNICEF brings value to this innovation in a number of ways, in terms of identifying the need for and ideal characteristics of rapid ZIKV Dx, and bringing solutions to scale, including:

- SD is well positioned to **understand needs and global demands** for novel products (one IRB), and the **needs of product developers**. Identifying the need for rapid ZIKV Dx and the specifications required for use in programme countries was an important component of this project, as SD took on the role of convener, providing direction to developers and manufactuers. The importance of acting as a convener is evident in contrast to the response to the Ebola virus outbreak, during which lack of understanding of needs and guidance from development partners may have resulted in a delayed response from manufacturers (two SD). Despite the availability of a TPP to guide product development,[34] individuals working with WHO during the epidemic identified several lessons from their experience with vaccine and diagnostic TPPs. These included the need for creative funding strategies (lacking in the case of Ebola virus response) to ensure that products move efficiently from research to clinical trials and manufacturing, and the need for coordination of the approval processes for clinical trials.[35, 36] The need for new funding strategies reflects the likelihood that public attention and the need for diagnostics and vaccines for Ebola virus and ZIKV may decline over time. Funding models such as the availability of an APC for rapid ZIKV Dx could fill this gap, meeting the needs of and providing incentive to the private sector for product development where future demand is uncertain. Further, contracting LSHTM will help to meet the needs of product developers related to clinical trials.

- SD offers value through its **procurement power**. The ability to leverage its signficant financial flows (US$3.5 billion) allowed SD to effectively signal to industry the market potential of rapid ZIKV Dx. Communicating to the market that there was a product SD was willing to purchase allowed developers and manufacturers to see value and commit additional resources to ZIKV Dx R&D (one SD, one partner).

  Insights: SD also provides value to this innovation to product developers and manufacturers, as described in the evaluation framework response to question 24.

10. What principles or standards have been applied and how?

Application of the Principles for Digital Development are not applicable to this innovation. However, SD follows its **procurement policies**, which are in place to ensure value for money, economy and effectiveness, and avoid perceived conflicts of interest and/or the appearance of endorsing one company over another.[37] SD also requires that manufacturers follow the **UN Supplier**

[34] World Health Organization, 'Target Product Profile for Zaire ebolavirus Rapid, Simple Test to be used in the Control of the Ebola Outbreak in West Africa', 2014.
[35] Osterhold, Michael, et al., The Ebola Vaccine Team B: A model for promoting the rapid development of medical countermeasures for emerging infectious disease threats', *Lancet Infectious Disease 16:e1-9.*
[36] World Health Organization, Evaluating Therapeutic Interventions against Ebola: Challenges and lessons learned – Perspectives from WHO, 9th European Congress on Tropical Medicine and International Health, 2015.
[37] United Nations Global Marketplace, 'Supplying the UN System', 2018.

Code of Conduct, which includes considerations for human rights, environment and anti-corruption.[38]

11. What are the steps taken or methods used to assess and mitigate risks to children, users, and markets?

SD has mitigated risks to children and users for this project through regulatory approval requirements, and the requirement for clinical evaluation through LSHTM.

5.2 Organization dimension

12. What type of support was received from the leadership to enable the innovation process?

The **SD Director's Office encouraged involvement of SD in the response to the ZIKV outbreak**, following which SD got involved with TPP development that was ongoing with WHO, PAHO and FIND. Further, the **IRB, being the only decision-making body in the PIP process, includes leadership-level membership** within SD.

13. What type of support and leadership facilitated the enabling environment for innovation?

A major success in facilitating an enabling environment for innovation at SD has been the **creation of an internal structure for innovation work**. SD has developed a unique, robust methodology for innovation that provides an internal structure to the process of innovation, while simultaneously providing developers and manufacturers with the flexibility needed to develop novel products that are fit for purpose, responding to an unmet product need in UNICEF programmes. However, based on feedback collected through this case study, it is difficult to determine whether the IRB's role is more active or procedural.

- Innovations undergo ongoing review at the leadership level, **providing opportunities for critical reflection and input on what is and is not working**, and changes that need to be made. In the case of the ZIKV Dx PIP, the IRB fills this function. In cases where the board has no longer seen value in a PIP in the past, it has closed projects (one IRB). Being composed of Centre Chiefs, the relevant technical centre lead brings in-depth knowledge of the innovation to the group. The addition of the Products and Markets Advisory Board further strengthens the subject matter expertise of the board, as it will support IRB decisions. In addition to providing input on PIPs from a number of perspectives, membership of the board provides leadership support and buy-in to product innovations.

- The governance structure of the PIP provides various **entry points for stakeholders with different subject matter expertise to provide insight** on the project. The formal stage-gated structure used by SD for PIPs seeks and requires guidance and insight from industry, the IRB and PRG at various points over the lifecycle of an innovation. Input from the groups creates opportunities for realignment, challenges assumptions, and improves likelihood for innovation success. However, based on interviewee feedback, decisions made at the level of the IRB may be procedural, and lack the debate and discussion intended through the structures developed (two SD). This may especially apply to projects responding to a crisis such as the ZIKV outbreak, requiring rapid decision-making. In cases such as these, the IRB may be less influential than for typical product innovations.

- Significant investment of time and resources in projects at the leadership level can help to advance projects more smoothly through the innovation process, but **political investment could create challenges to closing projects at the appropriate time**. For example, governance and membership of the IRB may create challenges in the future, if ZIKV Dx are no longer needed and the project therefore not viable (two SD). The IRB does not typically hold a vote to determine next

[38] United Nations, 'UN Supplier Code of Conduct', 2017.

steps for PIPs presented, which has been flagged as a potential issue if members do not counter decisions to proceed with projects that should be closed (one SD). This risk should be minimized by the requirement for products to meet checklist criteria prior to passing through stage gates. While, for instance, in the Stage Gate 1 Proposal, PIPs must define a problem statement, value proposition, project outcomes and outputs, business case and project plan, evidence suggests that criteria for project continuation and/or closure could be strengthened.

14. Who makes decisions with respect to the design and implementation of the innovation?

Decision-making regarding the design and implementation of the innovation is the responsibility of the IRB and Project Team, with input from the PRG.

- **IRB:** Composed of SD Centre Chiefs (as of 2018; previously was a smaller group that included representation from the Directors office, Evaluation, and Contracting Centre), the IRB is the only decision-making body in the innovation pathway for ZIKV Dx, and has purview of the overall portfolio. The IRB is the governance structure for SD PIPs, controlling advancement through the stage-gated innovation process. The board holds session monthly, during which PIPs can be presented to receive feedback during the project or to advance to the next innovation phase.

- **PRG:** Group of technical experts that provides direction and support to the Project Team at key inflection points along the innovation pathway (e.g., prior to publishing an RFP). The PRG works in an advisory capacity and does not have decision-making power, but brings valuable insight to the group (two SD). For example, debates raised at the level of the PRG have included probable geographic distribution of ZIKV in the demand forecast, whether a multiplex should be favoured over a singleplex diagnostic and independent assessment of responses to the RFP (two SD, one partner). The composition of the PRG provides additional levels and areas of subject matter expertise on which the Project Team can draw, strengthening its decision-making processes.

- **Project Team:** Responsible for day-to-day decision-making for the project. Major decisions and/or progression through the stage-gated innovation pathway used for PIPs are made at the level of the IRB; the Project Team presents its recommendations and/or gate proposal to the IRB for input and final decisions.

15. What factors were considered when making decisions about governance and ownership of the innovation?

Governance of the innovation follows the standard processes for PIPs. Ownership of the project falls to HTC, the Centre in which the Project Manager sits; however, levels of responsibility (e.g., between HTC, IU, MFSDU) for the project have varied depending on the phase of the project and the expertise required.

16. How has the governance and ownership model influenced the innovation process?

See question 13 for a description of the governance model and its influence on the innovation process, and question 19 for details on the influence of the ownership model.

17. To what extent was sustainability considered the plan for the innovation?

SD selected diagnostics for LTAs through a competitive RFP process, which is generally followed for PIPs in order to select the most appropriate and cost-effective product(s). The Procurement Strategy for ZIKV Dx 2017–2019 aimed to accelerate market availability of two novel products by December 2017, and five novel products by 2018. While the attainment of these targets has been delayed, the strategy aims to **promote a more healthy and competitive market for diagnostics**, thereby contributing to sustainable procurement.

18. When will this innovation become mainstream and no longer considered an

innovation? What steps has UNICEF taken to move toward that point?

SD uses PIPs to drive research, development, availability and scale, and the stage-gated process that is followed moves from the 'explore' through 'scale-up' phases. Therefore, ZIKV Dx will no longer be considered an innovation when the devices procured through SD are commercially available and reach scale (i.e., global demand).

19. How, if at all, has the innovation team worked across UNICEF offices and divisions to leverage internal and external knowledge and expertise and share learnings?

The project has **leveraged the capabilities of multiple internal groups**, including the HTC, IU and MFSDU. As the PIP has moved through the innovation process, the innovation team has evolved based on matching the knowledge and expertise of internal groups with project needs.

- **HTC:** Presented the Project Charter to the IRB for approval of the project as a PIP. HTC has coordinated the operations side of the project, which has included providing contracting and technical expertise, drafting the procurement strategy, preparing the tender, and evaluating responses to the RFP. HTC has also coordinated and hosted developer and manufacturer webinars and consultation with the PRG, in collaboration with other Project Team members.
- **IRB:** The sole decision-making body for SD's PIPs, the IRB is intended to provide input and make decisions on progression of the project at key points along the innovation pathway.
- **IU:** Engaged SD in co-development of the TPP and prospected the leads to identify the necessary funding from USAID to structure the appropriate financing for the APCs (with support from PPD). Leads the partnership with USAID (for this project).
- **MFSDU:** Designed the APC, in collaboration with HTC, to accelerate and de-risk investment and incentivize R&D of ZIKV Dx. Worked with HTC to design the procurement strategy and solicitation documents. Negotiated the structure and terms with PAHO (although unrealized), and jointly negotiated financing terms with PPD and IU to secure/lock down the financing from USAID.
- **PPD:** Supported MFSDU and IU to secure funding for the APC, assisting with preparation of the necessary documentation and support with internal processes. Leads overall relationship with USAID.

The **diverse composition of the Project Team** has strengthened the outputs of the project. For example, two key members of the Project Team are a Contracts Manager and Technical Specialist. The Contracts Manager was able to bring valuable insight to the project from a procurement perspective, complemented by the technical expertise provided by the Technical Specialist. Involvement of the IU and MFSDU throughout the innovation pathway has also strengthened the project by leveraging internal expertise in areas such as innovative financing mechanisms.

Insights: Taking a systematic approach to **needs identification at the country programme level** could strengthen the innovation process for future PIPs. Based on feedback, many ideas for PIPs come from SD headquarters and/or external actors (e.g., product developers and manufacturers); however, interviewees (one SD, two IRB) expressed that product innovation should ideally be driven by UNICEF Country Offices (COs) and/or other Divisions through the local identification of gaps. COs are largely unsure of how to engage in product innovation (e.g., through identification of needs, or field trials), as there is little awareness of the innovation work SD completes.

Identification of issues at the country level for which a new or improved product could offer a solution could improve product design through input on specifications that reflect local contexts. While the ZIKV Dx project was in response to a public health emergency that was identified as a priority at headquarters level, greater consultation and engagement with other divisions and/or offices within UNICEF (e.g., PD, COs, ROs)

could have strengthened understanding of local contexts and needs, and improved the potential for successful implementation and scale-up at the country/programme level.

5.3 Resources and capabilities dimension

20. How is the innovation funded?

The US$10 million **APC is funded by USAID**. While USAID is not typically able to provide funding in this capacity, the emergency status of the outbreak provided an opportunity to explore financing mechanisms new to the organization, with little resistance (one partner). International pressure and urgency to respond to the ZIKV outbreak, and threat of ZIKV spreading to other regions including the United States, allowed SD and its partners to respond quickly, and incentivize product development in new ways. See question 25 for details.

The IRB has an annual budget of US$500,000, which is spent on a variety of PIPs for activities, including field trials, travel and industry consultations. The **budget for ZIKV Dx project activities** is partly funded through this amount, which covers project activities including clinical evaluations, supplier meetings and travel for the PRG.

21. How much time and how many resources were invested at different points in the innovation process?

The **estimated budget in 2016** was between US$247,109 and US$823,339, including salaries for a Project Manager anchored within the Innovation Unit, a diagnostics technical specialist anchored in the SD Health Technology Centre (HTC), a Contracts Officer also anchored within the HTC, and a consultant that will provide technical input on the TPP to the HTC. Travel and expenses for the Technical Advisory Committee, a two-day supplier meeting, field trials of an RDT, and travel for the Project Team were also included. Of this estimated budget, the amount covered by the IRB during the exploration phase of innovation was US$92,958; these funds from the IRB were allocated to hire a Project Manager, complete the industry consultation prior to issuing the first tender, and travel costs associated with these activities. As of December 2018, financial values for the complete project are not available.

22. What ongoing resources (human, physical, and financial) are required from UNICEF to manage this innovation?

See question 21 for a breakdown of human and financial resources required from UNICEF.

23. How, if at all, have partners external to UNICEF contributed to the innovation process?

Partners external to UNICEF have made important contributions to several aspects of the innovation process. Key partners and their project roles and responsibilities include:

- **LSHTM:** After awarding LTAs for two products submitted through the first tender process, manufacturers had difficulties finding serum samples necessary to conduct clinical evaluations. In response, SD engaged LSHTM to **complete the clinical evaluations** on its behalf, **leveraging its network of specimen collection sites** (two SD, two manufacturers). One manufacturer awarded an LTA expressed during interviews that they were impressed with UNICEF's decision to engage LSHTM, following withdrawal of the WHO EUAL procedure for ZIKV IVDs, which complicated the regulatory approval process.
- **PAHO:** Involved in development of the TPP with WHO, FIND and SD. PAHO was intended to be a project partner and to procure on behalf of LACRO countries; however, the organization is no longer involved in the project.
- **USAID:** Provided a **US$10 million grant to fund the APC** to reduce demand uncertainty and guarantee procurement off-take for potential products. There was a strong consultative discussion between SD and USAID regarding design of the APC (one SD, one partner).
- **WHO:** Led the TPP development process, including hosting a meeting in March 2016 to plan accelerated development and

evaluation of products, including diagnostic tools to respond to the ZIKV outbreak in Southern America. WHO also established a EUAL Procedure for IVDs for ZIKV; however, EUAL listing was not included as a requirement for regulatory approval in the second tender process, since ZIKV is no longer considered a Public Health Emergency of International Concern.

24. How are partnerships designed to provide value to partners?

In addition to the value described in question 9, SD designed several components of the project to provide value to product developers, in order to incentivize R&D. SD does not enter partnerships with developers and manufacturers in alignment with its Procurement Principles; however, manufacturers interviewed described the following ways that SD has provided value to them through this project:

- **Availability of an APC:** SD and USAID offered value to developers and manufactuerers through the APC, which was designed to reduce the risk of investment in R&D. Based on feedback collected through a survey completed by the Project Team (two SD) and evalaution interviews (three manufacturers), the APC was highlighted as a key motivator for engagement with UNICEF, and reduced the risk for investment in R&D in ZIKV Dx, the market for which is niche and therefore presents greater risk to the developer (as opposed to product development for larger markets).
- **Opportunity to improve access to care:** One manufacturer awarded an LTA stated that development and future procurement of its diagnostic offered the opportunity to improve access to care in programme countries. UNICEF's global footprint and the ability to contribute positively to the field provided unique value.
- **Transparency:** One manufacturer stated that they appreciated that UNICEF maintains transparency throughout its procurement processes. This was noted through the tender process, including communication with manufacturers through the webinar and publication of responses to questions asked by manufacturers (two SD, two manufacturers).

25. What methods, approaches or tools are used throughout the innovation process?

Previous experience with product innovation has led SD to move toward **co-creation with industry through competitive procurement processes**, as independent product innovation requires significant expenditure for R&D of a prototype, and field trials among other activities. As a result, SD takes a **market-based approach to innovation**, communicating its product needs and inviting the market to respond. Outputs of the PIP, including TPPs and demand forecasts, signal to industry the need for product development, creating a business case for R&D.

- **Demand forecasts** demonstrated global demand and potential procurement levels through SD to product developers. See question 6 for details.

- SD utilizes **RFPs and TPPs** that are **less prescriptive** in order to **stimulate creativity** of product developers and manufacturers (one IRB). The TPP developed for ZIKV Dx provided developers with flexibility to develop a wide variety of products, all of which could potentially meet the specifications provided in the RFP. The inclusion of minimum acceptable criteria for diagnostics included in the TPP ensured that products developed would meet the needs of UNICEF and its partners for use in programmes; these were complemented by the inclusion of ideal product characteristics, which were more aspirational in nature. The ideal characteristics provided gave developers and manufacturers an idea of how products could be designed, but without describing an exact diagnostic tool. The resulting TPP provides a description of the ideal ZIKV Dx for programme use, but also provides space for product development to be done in a variety of ways, playing to the technical strengths of each supplier.

The ZIKV Dx PIP was the **first time that SD and USAID developed a pull mechanism (i.e., APC)** to accelerate market availability of novel products. While conclusions on the success of the pull mechanism cannot yet be made, as products selected from the first tender are just beginning to undergo field testing, certain insights on the use and outlook for the APCs have begun to emerge.

- The use of **alternative financing mechanisms** for innovation projects is itself innovative within UNICEF and USAID, and could be applied to other innovations with lengthy time to development and market uncertainty. The role of SD in development of ZIKV Dx was first to develop TPPs to ensure that R&D is focused on products that are fit for purpose in low-resource settings, and to design and implement a pull mechanism that would reduce the risk of investment in R&D. The use of APCs to signal demand (as estimated through development of the demand forecast developed by SD, WHO and PAHO, and validated by academia) and drive the market towards R&D for novel diagnostic products appears to be working and has been well received by industry (two SD, three manufacturers).

- **Design of financing models** for innovation projects can lag slightly behind the innovation, in order to be fit for purpose. Although not always ideal, in the case of ZIKV Dx the slight lag allowed greater time to understand the needs of the manufacturers and evaluate the appropriateness of available financing structures (one SD). During development of the Procurement Strategy for ZIKV Dx, the Project Team considered the need for a special contracting mechanism (employed when the use of normal tools will not work). After considering the risks to manufacturers and time requirements for diagnostic development, and in the context of developing a procurement strategy, SD decided to proceed with design of the APC.

- **Feedback from industry** was important to develop and refine financing structures that meet the needs of the target stakeholder group (e.g., manufacturers). While the original RFP did not explicitly define a target unit price, it did provide the financing available and maximum units to be procured, which implied a cost per unit. This received a reaction from interested developers and manufacturers, who communicated that the cost per unit would need to be doubled in order to be realistic from a supplier perspective (one SD). SD was then able to react to that feedback during selection of suppliers for LTAs for the first tender process. In the Procurement Strategy for 2017–2019, the target unit price for diagnostics is US$1.5 in 2017–2018, and US$1.0 in 2019; however, through the second tender process SD will procure up to 2M multiplex diagnostics and 0.5M singleplex diagnostics with up to US$7M remaining for the APC, which would result in a maximum unit price of US$2.8. This demonstrates a significant shift in the unit price up to which SD is willing to procure novel products.

- The impact(s) of the use an APC to accelerate market availability of ZIKV Dx is not yet known, but **the second tender is expected to provide an indication of its potential to drive development of new products**. Feedback from manufacturers that participated in the first tender has indicated that the LTAs and APCs were of value, demonstrating demand and transferring risk to a willing catalytic partner. However, the first tender attracted proposals for diagnostic tools that were already in the late stage of development, rather than encouraging R&D of entirely new products (or continued R&D in products that would otherwise have been abandoned). The results of the second tender should provide a better idea of the PIPs' ability to drive development of products that would otherwise not have been conceptualized or received the investment needed to drive R&D.

5.4 Incentives and outcomes

26. What incentives are encouraging/driving and discouraging/deterring adoption of the innovation by users?

Not applicable. Diagnostics selected for LTAs through the first tender process have not yet met completed clinical evaluations required for procurement through SD, and therefore have not yet been tested by end users and/or implemented at the programme level.

27. How were metrics designed and used to inform the development and scaling of the innovation?

Since SD's approach to this project is co-creation with industry through competitive procurement processes, the metrics designed reflect its role to accelerate development of novel diagnostics at a competitive price for use in programme countries. The PIP will contribute to SD **Supply Outcome Target #3**, the objective of which is to accelerate commercial availability of at least two RDT/POC IVD products for Ebola virus disease, ZIKV and other flavivirus infections by the end of 2020. The project also has several performance metrics included in its Procurement Strategy, against which progress toward strategic objectives will be measured, including:

- **Two novel diagnostics** available by 31 December 2017 *(delayed)*
- **Five suppliers** in the market by 2018, in order to facilitate movement towards a health and competitive market for ZIKV Dx *(delayed)*
- **In-country field-testing** facilitated in order to demonstrate effectiveness and acceptability of novel products
- **Target RDT price** of US$1.5 in 2017–2018 and US$1.0 in 2019, to improve affordability of diagnostics for use in programme countries, and increase chances of sustainable procurement.

28. At what point were metrics considered? How was impact measured before scaling (or how is it intended to be measured)?

At a high level, the project outcome (to accelerate availability of fit-for-purpose and value-for-money POC diagnostics) was considered when the Project Charter was developed. SD developed more detailed objectives and corresponding indicators as part of the Procurement Strategy, which it published in 2017.

29. How has data generated through the innovation process created value for UNICEF partners?

No data have been generated thus far through the innovation process; however, demand forecasts provide manufacturers with estimated potential procurement through SD, and results of clinical evaluations will provide important information on product performance.

30. How were workplans, processes, learnings and practices monitored, documented and shared within UNICEF and beyond?

The PIP process requires Project Teams to update the **Project Charter** each time it presents the project to provide an update to the IRB, or pass through the next stage-gate. The ZIKV Dx Project Charter includes an overview of the project, intended outcomes and outputs, the strategy, project plan (including a timeline for activities), and resource requirements.

In addition to workplans shared internally at SD, USAID and SD collaborated on a **knowledge-sharing paper** in 2018, focused on the use of pull mechanisms for global health R&D. The paper includes lessons from two projects at SD (ZIKV Dx and pneumonia diagnostics), and compares the circumstances in which the advantages of using pull mechanisms are strongest.

31. What does the ideal future state of this innovation 'at scale' look like?

In the Procurement Strategy for ZIKV Dx, **integration of diagnostics into countries' testing algorithms** will drive demand and scale-up outside of LACRO. SD is working with national governments in several programme countries, and COs and ROs to develop prevention and response plans for ZIKV. Ideally, at scale SD will be able to provide a reliable and uninterrupted supply of diagnostics, meeting procurement demands of countries.

32. How has this innovation considered and demonstrated development outcome/impact

objectives? To what extent does the innovation contribute (or have the potential to contribute) to equitable results for children?

Although the project has not yet demonstrated development outcome objectives, there are several indicators in place through which SD will monitor progress towards objectives. See question 27 for details.

6. CONCLUSIONS AND CONSIDERATIONS

The rapid ZIKV Dx project is intended to accelerate the development and commercial availability of diagnostic tools that are accurate, low-cost, and can be used at the POC in low-resource settings. After identifying the need and validating the demand for such a product, SD worked with PAHO, FIND and WHO to develop a TPP communicating a set of required and ideal product characteristics to industry to guide the development of novel diagnostics. Following the initial design of the TPP, a diverse Project Team within SD worked with USAID to design an US$10 million APC to incentivize and de-risk product research and development for manufacturers, which would be awarded based on the technical and commercial evaluation of a competitive procurement process. SD signed two conditional LTAs, including access to an APC, through the first tender process. A second RFP was issued in June 2018, of which the objective is to establish LTAs for the supply of rapid ZIKV Dx with US$7 million remaining for APCs.

Recent market analysis has identified a continued gap in diagnostic tests intended for use in resource-limited countries at the POC, demonstrating the continued relevance of the innovation project. Further, SD and its partners have adapted the innovation project in response to lessons learned from the first tender. For example, the decision to focus on multiplex diagnostics enabling differential diagnosis among related arboviruses will provide a comparative market advantage in terms of surveillance capabilities, in addition to continued relevance of products developed in the case that ZIKV becomes less of a global priority as diagnostics move towards commercial availability. The decision to contract LSHTM for clinical evaluations also demonstrates adaptability in response to lessons learned, as manufacturers selected through the first tender process faced challenges to obtain a well-characterized serum panel to validate their assays.

Going forward, demand generation will be essential to the success of the innovation project, in order to improve the chances of meeting forecasted demand and enhancing the sustainability of procurement. SD could work with PD, COs and ROs to build demand and buy-in for novel diagnostics at the country and regional level for detection and surveillance purposes. Demonstrating the effectiveness of APCs to drive the market towards the development of novel products will also be important, in terms of determining the value of applying similar models to other innovation projects. The results of the second tender may be an indicator of the ability of APCs to accelerate the development of products that would not otherwise have reached commercial availability, and demonstrate the ability of TPPs to drive development of products that are fit for purpose for use in programme countries.

Table 5. Practical considerations for ZIKV Dx going forward

Review whether pull mechanisms have driven development of products that would otherwise not have made it to market	Following completion of the second tender, SD should review the products submitted, and from which manufacturers. Things to note might include the phase of development from the first to second tender (if a repeat application), the number of new developers and manufacturers that submitted proposals in the second tender, and whether the APC has attracted proposals from non-traditional and local manufacturers that often lack the financial resources needed for R&D in this type of product.
Understand the acceptability of ZIKV Dx	Once products have received regulatory approval, SD could consider completing an acceptability study, to understand if diagnostics meet user needs in programme countries and the potential impacts of diagnostic results on infected individuals. Since there is no treatment for ZIKV and the health threats are mainly for the unborn children of pregnant women (or women attempting to have children), there may be cultural considerations for use of diagnostics, and how results are used (e.g., family planning, surveillance, diagnosis of other viruses using a multiplex diagnostic) may vary depending on the country.
Consider completing a cost-effectiveness study for diagnostics	Following completion of clinical evaluations by LSHTM and commercial availability of diagnostics selected through the first tender, SD could consider completing a cost-benefit analysis of implementation and scale-up of ZIKV Dx. This could provide a better understanding of the value of ZIKV Dx (e.g., singleplex vs. multiplex), and allow national governments and/or development partners to make informed decisions regarding if and/or how diagnostics should be purchased and used.
Explore options available to deliver ZIKV Dx to countries in Southern America	PAHO is no longer a partner in the innovation process for ZIKV Dx, which could present challenges to implementing and scaling use of products in countries in which demand and political will may be greatest. Strategies to deliver POC ZIKV Dx to Southern America when they are commercially available could include revisiting the relationship with PAHO, which, although no longer a project partner, could potentially procure on behalf of the region, or developing a new relationship with another procurement agency for diagnostics in the region.
Begin to develop a strategy for demand generation for ZIKV Dx to enhance sustainability	SD should begin to consider how demand will be generated at the country level, and whether it will engage other divisions within UNICEF and/or external actors. All stages of the innovation pathway should be designed with scale in mind to improve the chances of meeting forecasted demand and enhancing sustainability of the project. UNICEF could begin to work with COs and ROs to build demand and political will at the country level, encouraging government to allocate resources towards detection and surveillance of ZIKV and other arbovirus (if applicable) in the population.
Develop a framework to track and communicate results for children	The Project Team should consider developing a results framework and/or Theory of Change to define and monitor intended outcomes, and how they will contribute to improved programmatic results for children. The existing indicators for the ZIKV Dx project are market-based (e.g., number of diagnostics developed) without obvious links to how diagnostics will contribute to the improved protection of children's rights, basic needs and/or opportunities. A results framework and Theory of Change would help to define targets, and to communicate outcomes to project partners and externally, improving the visibility of the project and understanding of its purpose.

Table 6. Innovation at UNICEF

UNICEF's procurement power and reputation as a convener can generate buy-in for an innovation	Industry and partners see UNICEF as an effective convener of stakeholders, with significant procurement power. This can be leveraged to generate buy-in for existing and future innovations, as has been done by SD for ZIKV Dx through regular consultation with industry and partner organizations, during which the strategic advantage of working with UNICEF is communicated through tools such as demand forecasting.

Seek external validation of the need and/or demand for an innovation	After identifying the need for RDTs that could be administered at POC in low-resource settings, the Project Team and its partners developed a demand forecast and description of the type of product it wished to accelerate to market. While the model was not perfect, it signalled procurement potential for novel diagnostics to industry. Since little was known about ZIKV at the time, opportunities for industry and academia to provide feedback on projections and ideal product characteristics challenged the assumptions made by SD. Feedback from industry generated alignment and buy-in among stakeholders, and strengthened the project as a whole. A similar process could provide valuable insight and validation for innovation projects across UNICEF, and improve early buy-in and adoption by relevant stakeholders.
Ensure that innovations are fit for purpose by identifying the minimum and ideal characteristics needed to respond to a specific need	Following needs identification and validation, design of innovations should be fit-for-purpose and consider end-user(s) needs. For ZIKV Dx, SD, WHO, FIND and PAHO first developed a TPP that described the minimum (i.e., necessary) and ideal characteristics of a diagnostic tool for use in UNICEF programmes. The basic requirements and 'nice-to-have' characteristics are intended to guide industry to develop the ideal product for use in low-resource settings by health workers with limited training. The minimum requirements ensured that the product would be able to achieve the intended results, while the ideal characteristics would serve in a more aspirational capacity without being too prescriptive, providing room for innovation and creativity among developers.
Utilize an internal structure for innovation with opportunities for meaningful engagement	The stage-gated process for innovation developed and used by SD is intended to give structure to the process, providing opportunities for reflection and input from internal (i.e., IRB) and external (i.e., PRG) stakeholders outside of the Project Team at critical points along the innovation pathway. Use of this type of governance structure could provide greater rigor and improve the chances of success and sustainability of innovation projects; however, based on interviewee feedback, in the case of the ZIKV Dx project, there may be opportunities to strengthen governance processes, and more meaningfully engage structures like the IRB for informed decision-making, ensuring that their roles are not simply procedural.
Find the right partners for innovation, with a common vision and selected approach	There were challenges early on with partner relationship management due to different opinions on the approach to responding to the ZIKV crisis. In this case, the partner did not agree with SD's preference for a multiplex diagnostic or exclusion of Brazil ANVISA as an accepted regulatory authority, and there was greater prioritization of on-the-ground response to the health crisis in Southern America. These challenges slowed progress towards issuing the first tender, and resulted in loss of a project partner that would have provided greater access to the market for which there is the greatest need for ZIKV Dx. In order to avoid delays and uphold valuable and strategic partnerships, UNICEF and its partners should agree on the vision and approach for the innovation prior to any major commitments by either partner.

ANNEX A: METHODOLOGY

Case study objectives

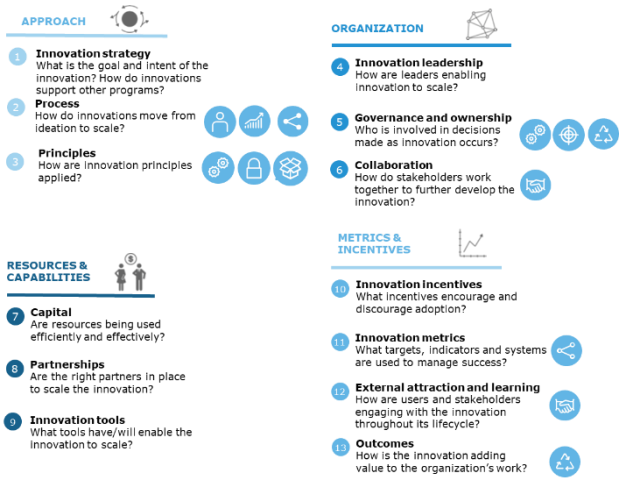
UNICEF approaches innovation as a strategy to tackle complex challenges faced by children around the world. For this reason, UNICEF identifies, field trials, and uses innovations to address bottlenecks or product gaps, thus **achieving results** that reduce inequities for children.

UNICEF commissioned Deloitte to conduct case studies to examine innovation across the spectrum of innovation types, country contexts, and internal (UNICEF) and external (partner) actors. Cases are **descriptive and explanatory**, identifying how the innovation process has played out in single instances and surfacing key issues, lessons, challenges and successes. During scoping and development of the Terms of Reference for this evaluation, cases were selected by the UNICEF Evaluation Office (EO) through a multi-step approach. While diversity across cases was considered as a factor for selection, the sample selected was not intended to be fully representative of innovation at UNICEF. The primary focus of this case is to understand the process of innovation for rapid ZIKV diagnostics (ZIKV Dx).

Evaluation framework

Evaluation questions were structured around a modified version of the Deloitte Doblin Framework for Innovation. Within this framework, the approach to innovation must be enabled through four thematic dimensions, including: approach, organization, resources and capabilities, and metrics and incentives. The four dimensions highlight the elements necessary to enable successful innovation. They are complementary to frameworks such as Supply Strategies and Public Procurement Principles.

Figure 4. Deloitte Doblin Framework for Innovation



Data collection approach

Deloitte employed a mixed methods approach to build a complete picture of the innovation process and identify findings related to the four thematic dimensions of the evaluation framework. Both qualitative and quantitative data were collected through desktop review and case study informant interviews.

Desktop review	• **Primary and secondary sources.** Conducted a review of demand forecasts, industry consultation documentation, presentations, workplans, budgets, Target Product Profiles, Requests for Proposals, and Innovation Review Board documentation. • **High-level organizational scan.** Reviewed UNICEF Supply Division documentation related to Product Innovation Projects and the stage-gated process of innovation.
Stakeholder engagement	• **Interviews.** Conducted semi-structured interviews, guided by interview protocols, with rapid ZIKV Dx Project Team members, IRB leadership, partner organizations, and developers and manufacturers. • **Observations.** Field visit to the Supply Division in Copenhagen, Denmark, to meet with key UNICEF stakeholders.

Description of field visit activities

Two evaluation team members conducted a field visit to Copenhagen, Denmark, from 11 to 14 June 2018. The evaluation team prepared guidance on the types of stakeholders to be engaged during the visits. The UNICEF Supply Division (SD) aided in the selection of specific stakeholders and logistics for field visits. Key activities included interviews with key SD stakeholders across four case studies, one of which was rapid ZIKV Dx.

Limitations of this case study

- **This evaluation does not systematically assess the impact or outcomes of innovation.** Evaluative case studies capture perspectives on potential outcomes and impacts of innovations, when appropriate. However, given the early stage of development, limited scope of engagement and rapid approach to conducting the cases, the evaluation does not make objective conclusions on outcomes or impact related to rapid ZIKV Dx.
- **A single case is not representative of the total population of innovations at UNICEF.** The sampling methodology for selection of cases (i.e., number, type, and field visit locations) was not randomized and, due to the highly qualitative and contextual nature of case studies, findings from this case are not generalizable to innovation at UNICEF. As such, cross-case analysis performed by UNICEF should be done taking this limitation into consideration.
- **Field visits were intended to reflect the innovation, rather than the SD.** As such, these case studies will not make inferences on SD's overall performance in innovation or on the impacts of its innovation function.
- **Due to the nature of innovation, it is expected that some innovations will continue to evolve during case study implementation.** This case presents a reconstruction of the innovation process up to June 2018. Future activities and priorities shared by stakeholders will be captured, but cases will not strive to make forward-looking statements or conclusions.
- **Potential for positive bias in documentation received from SD.** It is noted that SD has a strong process in place for documentation of progression of Product Innovation Projects (PIPs). However, the majority of documentation received was developed and used by Project Team members and could be positively biased. Where possible, external sources, including documentation and interviews, were reviewed to validate findings from document review.
- **Potential for bias from case study informants.** Due to the limited nature of this case study, perceptions of stakeholders who were not involved in the process of development of the rapid ZIKV Dx PIP were not collected. As a result, perspectives of individuals with a stake in positively framing the innovation process are primarily presented. To minimize this bias, external sources of documentation were consulted to verify interviewee statements where possible.

ANNEX B: ZIKV DX STAKEHOLDERS

UNICEF Supply Division, PAHO, WHO, USAID and developers and manufacturers have been involved in development of ZIKV Dx at various points along the innovation pathway. The London School of Hygiene and Tropical Medicine (LSHTM) has been engaged to complete a clinical evaluation of the two products selected for LTAs from the first tender, beginning in May/June 2018.

Table 7. Key organizations, role in development of ZIKV Dx, and status of engagement over the course of the evaluation

ORGANIZATION	ROLE IN ZIKV DIAGNOSTICS	ENGAGED?
UNICEF Supply Division	UNICEF SD will act as the procurer of ZIKV Dx, and the innovation process will follow the stage-gated process utilized for product innovations. Involved in development of the TPPs to guide industry and define requirements for ZIKV Dx.	YES
Innovation Review Board	Composed of SD Centre chiefs, the IRB is the only decision-making body in the innovation pathway for ZIKV Dx, and has purview of the overall portfolio. The IRB is the governance structure for SD PIPs, controlling advancement through the stage-gated innovation process. The board holds session monthly, during which PIPs can choose to present to receive feedback during the project or to advance to the next innovation phase.	YES
Procurement Reference Group	The PRG operates in an advisory role for the innovation, without decision-making abilities. The expert group has provided insight during the development of the tender, selection of developers and manufacturers for LTAs, and design of the APC.	YES
USAID	Provided US$10 million grant to fund Advance Purchase Commitments (APCs) to reduce demand uncertainty and guarantee product off-take for potential developers and manufacturers. Involved in development of the TPPs to guide industry and define requirements for ZIKV Dx.	YES
PAHO	Involved in development of the TPPs to guide industry and define requirements for ZIKV Dx. Was originally intended to procure on behalf of LACRO countries. PAHO is no longer involved with the PIP.	NO
WHO	Launched the inter-agency ZIKV Strategic Response Plan (SRP) in 2016, and held a joint WHO/UNICEF-led industry consultation. Involved in development of the TPPs to guide industry and define requirements for ZIKV Dx.	NO
LSHTM	A key step in development of diagnostic tools is clinical evaluation. Manufacturers identified challenges securing serum (i.e., blood samples) for testing, so the LSHTM will conduct lab-based validation. The service agreement covers development of reference materials and evaluation of product performance against manufacturer claims, through access to its network of specimen collection sites.	NO
Product developers and manufacturers	Developers and manufacturers are expected to accelerate or develop novel products for ZIKV Dx in response to the pull mechanism. Suppliers awarded an APC would establish LTAs with UNICEF, including guaranteed off-take in the case of reduced need for ZIKV Dx.	YES

Table 8. List of interviews completed for this case study

Name	Organization	Position
Gian Gandhi	UNICEF SD	Chief Markets, Supplier Financing and Innovation Centre
Kristoffer Gandrup-Marino	UNICEF SD	Chief Innovation Unit
Nagwa Hasanin	UNICEF SD, IU	Senior Advisor, Health Emergencies
Jonathan Howard-Brand	UNICEF SD, IU	Innovation Specialist
Natalie Jones	UNICEF SD, IU	Operations Officer
Jay Kang	SD Biosensor, Inc.	Manager of International Organization
Sharon Klugewicz	Chembio Diagnostics Systems, Inc.	President, Americas Region
Jonathan M. Weiss	UNICEF SD	Chief Procurement Services
Gemma Orta-Martinez	UNICEF SD	Chief Monitoring, Strategic Data and Evidence Unit
Ana Cristina Matos	UNICEF SD	Evaluation Specialist
Lama Ramzi Suleiman	UNICEF SD, HTC	Malaria Prevention & Diagnostics Unit / Contracts Manager
Suvi Rautio	UNICEF SD	Deputy Director Supply Programme
Priya Sharma	USAID	Senior Policy and Innovative Financing Advisor at the Center for Accelerating Innovation and Impact
Cedric Sungho Jo	SD Biosensor, Inc.	Regional Manager, International Sales Department
Regine Weber	UNICEF SD	Chief Strategy, Change and Communications Centre

ANNEX C: LIST OF DOCUMENTS CONSULTED

List of UNICEF files shared with the Evaluation Team

- Sharma, P., A. Lin, R. Fowler and K. Gandrup-Marino, 2018. Pull Mechanisms for Global Health R&D (Manuscript Draft).
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ANNEX D: THE CONTEXT FOR INNOVATION AT SUPPLY DIVISION

Supply Division (SD) Product Innovation Projects (PIP) are intended to create impact for women and children through UNICEF programmes, and follow a defined process that covers all stages of innovation, from idea to implementation and scale. SD designed the procedure to facilitate an iterative approach to innovation that is valuable and flexible, with effective governance for each individual PIP.

Innovation process: Supply Division has defined a stage-gated innovation process to cover all stages of the PIP life cycle, from exploration to scale. The process is meant to be highly iterative at the beginning of the PIP in response to new information and/or lessons learned, with decreasing levels of iteration as the project progresses.

GATE	Phase 0: Explore	GATE	Phase 1: Concept	GATE	Phase 2: Field trial	GATE	Phase 3: Scale up
Description	In this phase, the Project Team will conduct research to assess relevance, complete a needs assessment and user analysis.		This phase explores and tests potential solutions to address the challenge, including detailed analysis of concepts and development of a draft TPP.		In this phase, the physical prototype(s) of the product is developed and tested in the field, and may involve multiple iterations.		In this phase, scaling of the solution(s) begins through increased procurement and close monitoring of implementation.
Level of iteration	High		Moderate		Little		Very little

To advance from one phase of innovation to the next, PIPs must meet the criteria required to pass through a stage gate. A PIP may start and be closed at any gate/phase of the innovation process.

Governance of the innovation process: In order to pass through Gate 0 and enter the exploration phase, the Innovation Chief and Centre Chief must approve a project as an innovation. Following approval as a PIP, advancement to the next phase of the innovation process requires the project to pass through a stage gate after presentation of its status to the Innovation Review Board (IRB). The IRB is the sole decision-making body for PIPs, responsible for deciding whether a product should advance to the next stage of innovation, remain in the same stage, or be abandoned. The Project Team presents the status of PIPs at meetings of the IRB at key points in the life cycle of the innovation, for example, to obtain resources for field testing, or to receive input on significant decisions.

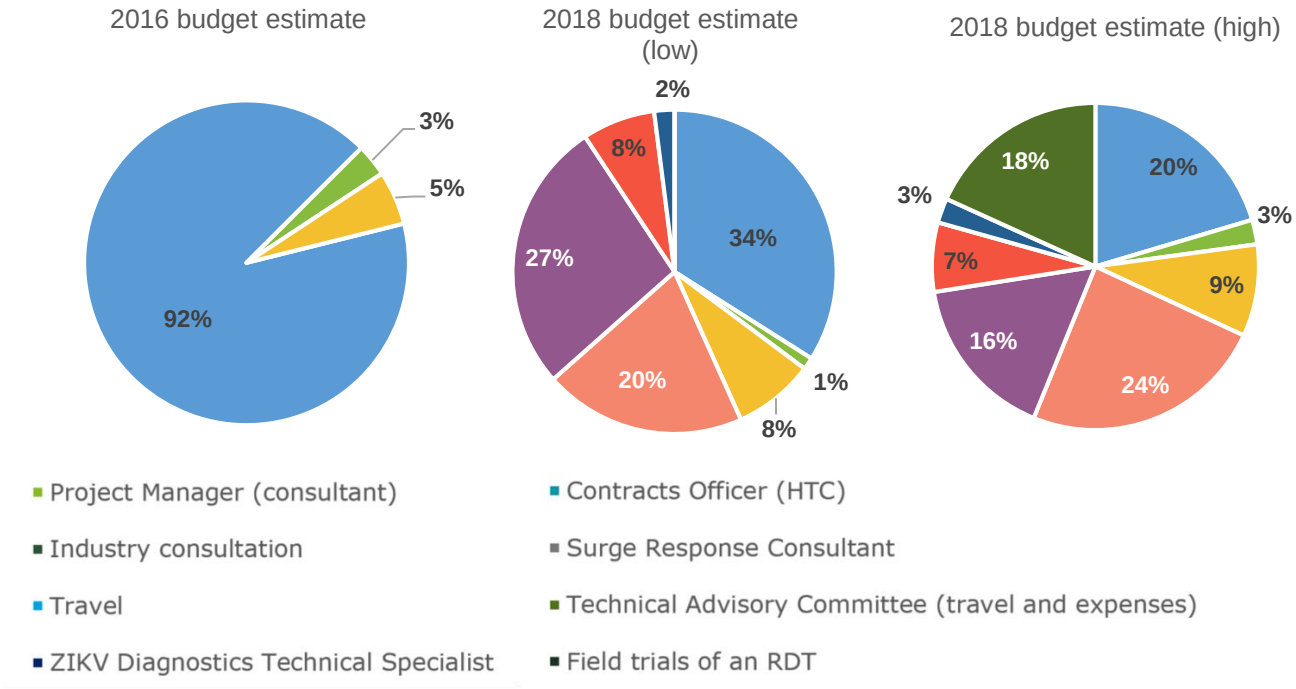
Documentation: Advancement through the phases of innovation is well documented at each stage of the project life cycle, and typically includes:

- Project Charter
- IRB Budget Template
- Project updates to the IRB
- Gate proposal (case for passage through each gate)
- Presentation to the IRB (for input and/or passage through each gate)
- IRB minutes.

ANNEX E: FUNDING FOR THE ZIKV DX

The IRB has an annual budget of US$500,000, which may be spent on a variety of PIPs for activities including field trials, travel and industry consultations. For example, IRB-approved spending for ZIKV Dx includes a budget for hiring a consultant with technical expertise in diagnostics to evaluate supplier proposals during the tender process.

Figure 5. Budget allocations for ZIKV Dx Product Innovation Project



The budget for the ZIKV Dx PIP in 2016 during the exploration phase of innovation was US$92,958, which was allocated to hire a Project Manager, completing the industry consultation prior to issuing the first tender, and travel costs associated with these activities.

The budget estimate for 2018 has increased significantly from the exploration phase, to between US$247,109 and US$823,339, as the project has moved to the next stage of the stage-gated innovation process. Notably, SD will issue the second tender and begin field trials for the rapid diagnostic tests selected for procurement during the first tender. Due to increased activities, resourcing requirements for 2018 include a Project Manager anchored within the Innovation Unit, a diagnostics technical specialist anchored in the SD Health Technology Centre (HTC), a Contracts Officer also anchored within the HTC, and a consultant that will provide technical input on the TPP to the HTC.

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