

**The POC Market for Diagnostics of Diabetes, Maternal and Child Health,
Tuberculosis, Malaria and Diarrhoeal Diseases in India and the World**

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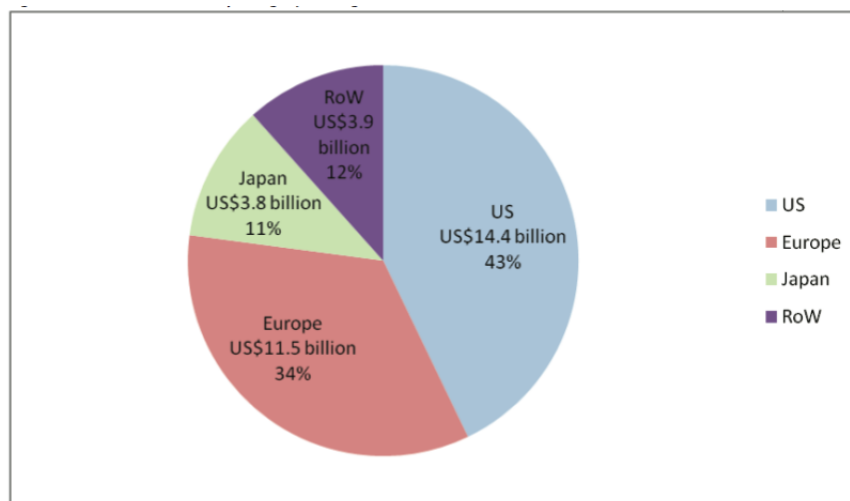
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This paper intends to introduce the market of point-of-care (POC) in diagnosis of diabetes, tuberculosis, malaria, diarrhoeal diseases and maternal and child health. A description on the complete spectrum of diagnoses and treatments of the five medical cases is beyond the scope of this paper. Rather, the study merges statistical information on the diseases with the relevant POC tests.

Introduction

Point-of-care testing (POCT) is any testing performed outside of the traditional, core or central laboratory and conducted close to the site of patient care, typically by patients or clinical personnel whose primary training is not in the clinical laboratory sciences¹. Technological advances over recent years have helped POCT evolve into a vital diagnostic tool, and have expanded the medical diagnosis field to operate in every patient treatment setting. POCT is expected to expand dramatically in the next couple of years. For instance, the POC market in 2007 was estimated to be worth US\$11.32 billion, and is forecasted to reach US\$18.85 billion by 2012, growing at around 11% a year. It is thus a critical component of the global in-vitro diagnostics (IVD) market¹.

There are several factors that motivate the expansion of the POCT market, including aging populations and increasing rates of obesity. Obesity and older population have led to higher rates of chronic diseases that require frequent testing, such as coagulation analysis and blood sugar. Even though obesity and aging population rates have a global impact, most of the POC testing market is centered in the developed countries. The POC testing market in the U.S. is the most mature and developed POC market around the world. In 2007, it was estimated at US\$5.43 billion, accounting for 48% of the global POC market.



Source: Espicom estimates

Figure 1: Global IVD Market by Geographic Region 2007 US\$33.6 Billion

The most conventional and frequently used diagnostics are performed in specialized labs. While lab tests are cheap and accurate, it may take hours or even days to get results, leading to low efficacy levels. On the other hand, POC tests shorten significantly the time to diagnosis and results can be obtained immediately, or within 20 minutes. At the same time a treatment strategy can be chosen and started based on these results, thus, increasing likelihood of a follow-up and accurate therapy. POC diagnostics make a patient's treatment more convenient and as such POC can lead to dramatic improvements in the health condition of the Indian population that suffers from deadly chronic infectious diseases as diabetes, tuberculosis, malaria and diarrhoeal diseases.

While the improvements that POC can bring about are abundant, there are economic and technical challenges that also need to be addressed. Centers with remote diagnostics technologies (RDT) entail high fixed costs that include initial purchase cost, cost of interfacing POC devices with host information management systems as well as cost of management of POC diagnostics by coordinators. As a result, costs per tests in POC sites are higher than the costs for the diagnostic

procedure in the lab and there is little proof for their financial superiority. On the technical aspect, POC tests are susceptible to inaccuracies, as operators are often less skilled as compared to lab and hospital technicians. However, the financial and technical challenges can be tackled with better technology and improved staff training.

Malaria

Statistics

Worldwide, approximately 300 to 500 million people contract malaria annually, resulting in over one million deaths. Malaria, dengue and other vector-borne conditions were estimated to account for 1.6% of India's total disease burden, which is 4,200,000 disability adjusted life-years, yet it is likely to assume that these predictions are underestimates of the disease's spread due to underreporting by officials, information loss from private clinics and irrelevant diagnosis by household surveys⁶.

It is estimated that the deaths caused by the diseases will substantially decline for both sexes. While malaria was the 12th global killer in 2002, it has been estimated that by 2030, the disease will decrease to the 22nd biggest cause of deaths around the world. However, it will remain the 10th killer of people in low income countries⁵. The epidemiological differences between high and low income countries are also noticeable in the estimates of malaria's share of disability adjusted life years (DALYs). It has been estimated that globally, between 2002 and 2030, the disease will decrease from the 9th to the 15th rank, yet in low-income countries in 2030 malaria will once again reach the 10th leading factor for DALY's. To conclude, while disease estimates for high income countries show positive trends, the disease still remains a major health concern for third world countries.

POC tests

Currently, POC tests for malaria provide suboptimal results. The rapid result tests have not been evaluated yet, and some of the tests are not suitable for disease-endemic areas as they require long hours of incubation. In addition, clinical trials of malaria dipstick fell below expected levels of accuracy⁴.

Innovation in POC tests – Reports exist on several innovations of POC tests of malaria. For example, *Hema Diagnostics Systems* developed POC diagnosis devices for malaria that are suitable for low budget testing points. *Hema Diagnostics Systems* offers 3 products for the diagnosis of malaria that detect the species responsible for most cases of malaria morbidity. The immunoassays are noted for professional in-vitro use only. Thus, the adaptability of these tests to the level of professionalism in RDT sites is unclear.

In addition *BioSign* offers *Rapid Malaria Antigen Test* and *Trinity Biotech* produces *Uni-Gold Malaria*, both detecting the presence of malaria antigens in the blood, that provide accurate malaria diagnostics rapidly and are easily operated². *BinaxNOW* test is the first and only rapid malaria test available in the US, and is a simple, three-step test providing results within 10 minutes¹. In addition, *AT First Diagnostic* recently developed a new patent pending, micro lateral flow-through system used in the *FirstVue* brand line. Most tests are easy-to-perform, single-use screening tests for the rapid, visual detection of antibodies on a strip encased cassette. This format provides a test that is simple, rapid, safe, and shelf stable (18 month shelf life) and highly reproducible².

Tuberculosis

Statistics

Nearly 40% of the Indian population of all ages has *Mycobacterium tuberculosis* infection and there are about 85,000,000 people with TB at any given time⁶. With more than 400,000 dying each year, TB is the single most important cause of death in India at present. In 1998 TB accounted for 7,577,000 DALYs, which is 2.8% of the total burden of disease in India. TB Infection rates in India are also very high and amount to 1.8 million new cases every year¹.

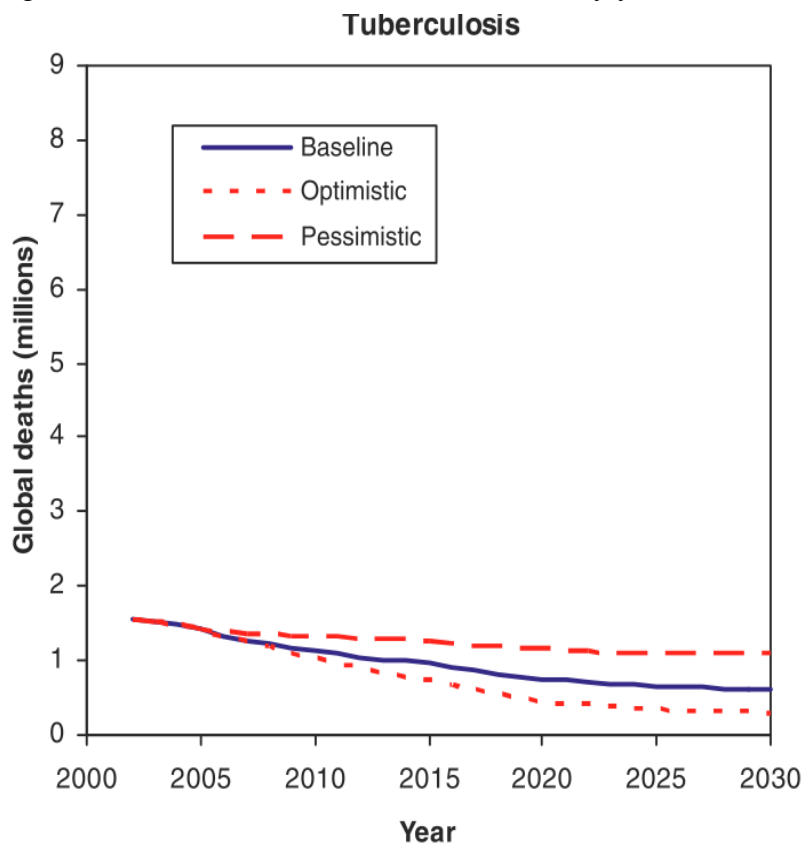


Image 2: Predicted global death rates from TB between 2002 to 2030

TB is also a major cause for deaths globally, and was ranked as the 8th leading cause of deaths in 2002. Under certain assumptions, it has been estimated that by 2030, TB will have a smaller impact on global human mortality and would be the 23rd leading cause of deaths. In addition, globally, the disease will decrease its share of DALY's from the 10th leading cause of DALY's to the 25th cause⁵. Even though these figures are uplifting, it is important to recognize that the statistics reflect the global state of tuberculosis, which is a combination of the polar situation of disease in rich and poor countries. As the disease is especially prevalent in poor countries, it is important to know the scope of TB there.

As TB is an infectious disease, POC TB tests and treatments can have an immense impact on the spread of the disease. It is estimated that an identification of positive TB cases before transmission to others followed by a directly observed treatment can reduce case-fatality rates resulting from smear-positive TB from 60%–70% to 5%⁶. A decrease in TB cases in India will have multidimensional effects. Rough calculations suggest that a reduction in mortality due to TB in India by one-half would raise the life expectancy of an Indian by 0.12 years and India's overall GDP by as much as 0.5%.

POC tests

Around US\$1 billion is currently spent on TB diagnostics annually, yet the most widely used method to diagnose active TB, sputum smear microscopy, has not changed substantially in 100 years, and is not very sensitive. The traditional methods of detecting active TB (e.g. smear and culture) suffer from procedural difficulties, lack of sensitivity and specificity, and are highly priced, thus limiting their application in many parts of the world. Other tests are currently available on the market such as T-cell-based assays and antibody-based assays. However, the sensitivity of these tests tends to be low, and is further reduced in patients who are immune-compromised (e.g. HIV-positive patients). In addition, the results are not immediately resolved and require laboratory conditions leading to a low efficacy level².

Innovations in POC tests – Several companies are developing products for the TB POC testing market. The Australian company, *Proteome Systems*, is creating a diagnostic test that will detect TB antigens, indicating whether there are active TB infections in the human body. The test will also monitor disease progression and response to treatment in patients with TB regardless of an HIV infection. *Proteome Systems* stated that the TB test would be an easily administered POC system, delivering an accurate result within minutes². *Hema technologies*, *BioSign* and *IND* diagnostic also offer TB tests that detect antibodies to active M. Tuberculosis in the blood system. *Hema technologies* and *IND* noted that the tests are in-vitro and should be used by professionals only². After winning Phase I and II Small Business Innovative Research grants from the National Institutes of Health from 1998 until 2002, *Chembio* is developing an accurate TB test that could diagnose TB for people who are infected or people not carrying HIV.

Diarrhoeal Diseases

Statistics

Diarrhoeal diseases account for 22,005,000 DALY'S, an astounding 8.2 % of the total disease burden in India⁶. Acute diarrhoeal disease is a major cause of childhood morbidity over the world, estimated to cause 600,000 deaths annually among children under five years¹. In projections on the development of infectious diseases, it is estimated that by 2030 diarrhoeal diseases will no longer be the 7th cause of death, but would be ranked in the 16th place. In addition, globally, the disease would also have a smaller share of the total burden of disease in India transitioning from the 5th position to the 12th cause. On the other hand, in low income countries such as India, the projections indicate a much worse scenario in which by 2030, the disease will still be ranked as the 8th cause of death in 2030 and the 7th leading factor for DALY's. Thus, diarrhoeal diseases show health inequalities between poor and rich countries and continue to induce heavy ramifications for third world countries. Adding to this prediction the fact that diarrhoeal diseases can be easily diagnosed and treated, there is great potential for a POC diarrhoeal market that would transform the diagnosis and treatment to RDT suitable methods.

POC tests

The current methods that are used to diagnose diarrhoeal diseases have limited accuracy and specificity and do not offer timely results. New tests that have been developed have low efficacy as they are highly expensive and require specialized instrumentations and trained technicians.

Innovations in POC tests – Despite the disease's magnitude, very little literature exists on the POC diagnosis market of diarrhoeal diseases. *Diarlex MB* developed a diagnostic test that detects rotavirus and adenovirus infections from a stool sample¹.

Maternal and Child Health

Statistics

Maternal and perinatal conditions are said to cause 31,207,000 DALYs, a share of 12% of India's total burden of disease. While there are no direct statistics on maternal and child health (MCH), by combining several reports on maternal mortality with infant and child disease prevalence and mortality, we gain an understanding on MCH. Infant mortality rates (IMR) and maternal mortality rates (MMR) have been extensively documented. IMR is estimated to be about 66 per 1000 live-births, yet the under-5 mortality rate was estimated at 95 per 1000 live-births in 1998–99 as per the National Family Health Survey – 3 in India. The maternal mortality ratio (MMR) was estimated at 440 per 100,000 live-births in 1992–96. A set of projections assume that rates of decline in the infant and under-5 mortality would be 46 and 62, respectively by the year 2015⁶. While studies predict that IMR would be lower than the goals laid down under the Millennium Declaration, the NCMH believes that these predictions are not accurate, and that in reality IMR would be higher than expected.

It is estimated that in the future, MCH diseases will have devastating ramifications, especially in poor countries, and as a result potential gains from interventions in MCH can be massive. According to NCMH estimates, a reduction in childhood mortality may raise the life expectancy at birth of an Indian by as much as 3.1 years, and India's Gross Domestic Product (GDP) from 4% to 12% .

MCH is a field that encompasses a range of diseases and cases that can be diagnosed and treated through POC products. Some products that promote MCH are pregnancy and fertility tests, as well as tests for cervical cancer, syphilis, HIV mother-child transmission and premature rupture of foetal membranes (PROM, known as ROM in the US).

Premature Rupture of Foetal Membranes – PROM may lead to infection and serious complications for the neonate and mother. It occurs in about one out of ten women, and is a major factor of pre- and post-natal complications. A diagnosis of PROM is important in any stage of the pregnancy and as such, PROM checks are fairly prevalent among pregnant women as about 30% undertake these tests. While ruptures are easy to detect with PROM diagnostics, the identification of occult ruptures must be done in specialized laboratories. In addition, the current PROM exams lack specificity and specialization and as a result they are not suitable for POC testing. Occult ruptures pose significant challenges for the NON POC market³.

N-Dia, Inc. developed the *AmniSure* Diagnostic test, a POC test for PROM. Through a non-invasive procedure in which sterile swab is inserted 2-3" deep, the test detects trace amounts of PAMG-1, one of the amniotic fluid proteins that appear in vaginal secretion after the membrane ruptures. *AmniSure* is an examination that is viable for RDT, as it claims to produce lab-standardized results rapidly, with minimal equipment and technical expertise, and can also be performed by nurses and midwives.

Cervical Cancer

Globally, cervical cancer comprises approximately 12% of all cancers in women. While it is the second most common cancer in women worldwide, it is the commonest in developing countries. In a report published by the WHO in 2002, it was estimated that there are around 470,600 new cases and 233,400 deaths annually from cervical cancer, while 80% of these cases take place in developing countries. There is no direct estimate of the potential product market size for cervical

cancer yet. *Matritech*, a developer of proteomics-based cancer diagnostic products, estimates that the worldwide potential product market for blood, urine and cervical cellular testing for bladder, cervical, breast, prostate and colon cancer testing could exceed US\$1 billion².

In 2002 the WHO noted that cytology, prevalent in middle-income countries, is the only established screening test for cervical cancer precursors that has been shown to reduce the incidence and mortality of the disease. Nonetheless, WHO also emphasizes that the test is not optimal for low-income countries, due to technologic and financial constraints and established the need for low-income cervical cancer diagnostics⁷.

SpectRx is a medical technology company focusing on the detection, monitoring and treatment solutions for the diabetes and cancer detection healthcare markets. The company is working on developing a non-invasive cervical cancer detection technology. *Matritech* is developing among other products, a diagnostic test for cervical cancer².

Sexually Transmitted Diseases

It is estimated that 12 million individuals are diagnosed with syphilis each year, and are at increased risk of becoming infected with and transmitting HIV¹. As these diseases can be transmitted from a mother to her unborn children, early and appropriate diagnosis is a major step in preventing the diseases' spread and providing appropriate treatment for the child and mother.

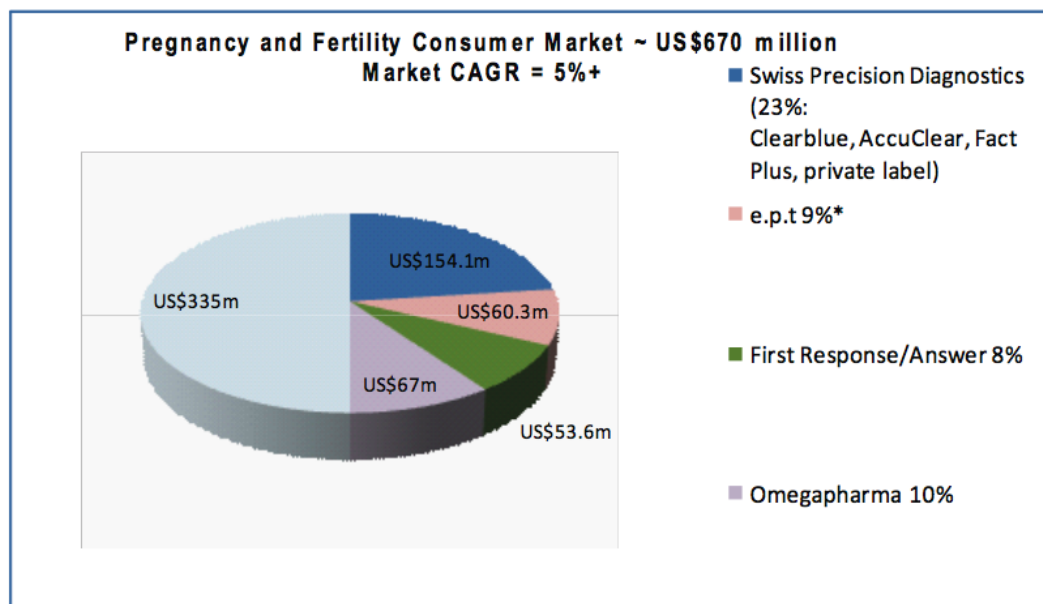
In 2006, *Chembio* Diagnostics signed an agreement with the United States Centers for Disease Control and Prevention (CDC) to develop a test for syphilis that could detect several antibodies, hopefully leading to a screening and confirmatory test in POC setting. Additionally, *Runbio-Tech* developed *One Step Anti-Syphilis Test* that aids the detection of syphilis. By detecting anti-treponema pallidum (TP) antibodies in serum, *One Step Anti-Syphilis Test* provides a rapid test (results can be read within 10 to 20 minutes) for the visual detection of syphilis in serum. No additional instrumentation or reagents are required. *BioSign Syphilis* by *BioSign* is another rapid Syphilis antibody diagnosis. *BioSign* is not as sensitive and specific as *Chembio's* initiative because it does not provide both screening and confirmatory information. *FirstVue* released the *inSTIcheck* that requires a single specimen to process and provide rapid results for STDs such as syphilis.

Multi-disease readers can be used for RDT's they are relevant for household POC. *Prima Biomedical* has produced *Multi UrinScreen Devices* that can rapidly produce quantitative determinations regarding various tests such as tumor markers, malaria, syphilis and HIV with a single specimen¹. It is important to qualify the adaptability of such multi-readers within RDT's as they may decrease costs of appliances and requisite technical knowledge on operation of several machines. Other syphilis tests should be handled by professionals and thus their relevance to RDT is not certain.

Pregnancy/Fertility tests

The global market for pregnancy self-tests has been increasing due to women's preferences for confidentiality of the pregnancy test results, the accessibility of the test, rapid results of the diagnosis and the convenience of testing at home. Pregnancy tests have the second largest POC market share, estimated in 2007 at US\$700 million and growing at a rate of 5% per annum over the period to 2012. Competition in the pregnancy detection and fertility/ovulation prediction market is intense, and includes a large number of large and small players. *Inverness Medical*, a global leader in POC, is the worldwide market leader for the consumer segment². There are numerous pregnancy

self-tests on the market, which are typically urine-based tests and provide results in less than five minutes.



Source: Inverness Medical estimates

*J&J e.p.t visual supply agreement began in June 2004 and e.p.t digital commenced Q4 2003

Figure 3: Global Pregnancy and Fertility Market

Diabetes

Statistics

In contrast with the projections on the future development of the previously covered diseases, diabetes mellitus is expected to rise due to higher obesity and overweight rates. Diabetes will have a greater impact on deaths and DALYs, moving, respectively, from the 11th spot in 2002 to the projected 7th position in 2030 and from the 20th rank in 2002 to the 11th position in the total disease burden in India in 2030. Moreover, the disease is projected to shed a greater impact on wealthy countries than low-income ones, as indicated by the ranking of causes of death in 2030 that situate diabetes in the 4th, 6th and 9th place, respectively, for high-income, middle-income and low-income countries⁵. On the other hand, overweight conditions and obesity are now dramatically on the rise in low and middle income countries, particularly in urban settings².

With an aging population and obesity, diabetes is expected to increase from 196 million cases in 2002 to 366 million cases by 2030². Given that continuous glucose monitoring systems are relatively new to the market, they currently only represent a tiny portion of BGM sales. They offer great potential for growth, especially through a wider uptake by insulin-dependent diabetics. The global blood glucose monitoring market enjoys the largest share of POC market, and was estimated to be worth US\$ 7.45 billion in 2007, and to grow to US\$12 billion by 2012².

It is estimated that 2.5 to 15% of annual health budgets are spent on diabetes-related illnesses. A reduction in the number of diabetes mellitus cases can lead to immense public and private savings,

and increase life expectancy by up to 20 years for Type 1 and up to 10 years for Type 2 diabetics². More specifically, according to the American Diabetes Association, the estimated economic cost of diabetes in the US in 2002 was US\$132 billion, of which US\$92 billion was related to direct medical costs.

POC Tests

Blood glucose levels are currently diagnosed by a small blood sample taken from the fingertips several times a day. However, less than 10% of patients with diabetes are known to frequently monitor their blood glucose levels, due to the inconvenience and pain associated with this method. On top of that, methods for glucose measurement are not utilized to their maximum as they do not track glucose levels when the patient is sleeping, and they can easily miss critical hypo- and hyperglycaemic events.

Innovations in POC Tests – Non-invasive continuous blood glucose monitoring (BGM) products are currently developed and if the financial and technical factors will be suitable for the RDT, the product could enter the consumer self-test market. *OrSense* developed the *NBM-200G* system, the first “truly” non-invasive test. Using optical spectroscopy to non-invasively measure glucose, haemoglobin and oxygen saturation, *OrSense* is focused on BGM for patients with a demanding need for glycaemic control in cases such as brittle, nocturnal and gestational diabetes.

Conclusion

The development of POC tests has a major potential to improve global health and to eventually reduce public and national spending on health. The projections for the POCT market show a rapid and dramatic growth and predict that by 2012 the global POCT market will reach \$18.85 billion, expanding at around 11% a year². The POCT market for infectious diseases such as malaria, TB, diarrhoea and STD will grow even faster at around 16% per year, and will reach US\$1.05 billion in 2012. On top of that, the market for blood glucose testing continues to increase, and is expected to reach \$12 billion by 2012, at an annual growth of 10%.

The health statistics of India present high DALY and morbidity rates, that can be countered through POC diagnostics and treatments for TB, diarrhoeal diseases, malaria, MCH and diabetes. As Indian health needs correspond with the POCT market’s expansion, there is a great capacity that should be tapped towards developing POC tests which are suitable for the Indian and global market.

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