**Device – Target Product Profile (TPP)**

**Health/Disease Area: Preterm Labour**

**Intervention/Candidate: Biomarkers to predict imminent preterm birth in women with symptoms of preterm labour**

# Version: <V1.0: 12 May 2025>

This is a draft document and is undergoing public consultation. It is anticipated that the contents and structure of this document may change during this process.

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# Background

## Preterm Labour and Birth

Preterm birth (being born alive at <37 weeks’ gestational age) remains a global public health challenge. Each year, an estimated 13.4 million babies – nearly 10% of all births – are born preterm, with the greatest burden in limited-resource settings.1 Preterm birth and its associated complications are the leading cause of death in newborns and children under five.2 The majority (approximately 91%) of preterm births occur in low- and middle-income countries, with around half (52.9%) in southern Asia and a quarter (28.2%) in sub-Saharan Africa.1 Most preterm births are spontaneous, with 40-45% due to spontaneous preterm labour and 25-30% due to preterm premature rupture of membranes (PPROM).3 The remaining 30-35% are provider-initiated preterm births.3,4

Babies who survive preterm birth are at increased risk of a wide range of morbidities – such as respiratory distress syndrome, cerebral palsy and infections - as well as poorer health and educational outcomes in the longer term.5 Earlier gestational ages at birth are associated with more severe health complications and increased need for specialised neonatal care.6

While most preterm births are moderate to late (between 32 to <37 weeks), around 15% are either very preterm (28 to <32 weeks) or extremely preterm (<28 weeks).1

## Prediction of Preterm Birth in Symptomatic Women

The World Health Organization (WHO) recommends several interventions to improve outcomes of babies born preterm,7,8 including administration of tocolytics to delay labour, administration of antenatal corticosteroids and transfer to a higher-level facility when necessary.9,10 Drugs can be administered antenatally - antenatal corticosteroids to accelerate lung maturation, magnesium sulfate for neuroprotection and prevention of cerebral palsy, and antibiotics to prevent infection – to improve preterm newborn outcomes.7

Symptoms of spontaneous preterm labour, such as uterine contractions and cervical changes, can signal the possibility that active preterm labour has commenced and preterm birth may occur imminently. However, fewer than 10% of women presenting with these symptoms give birth within seven days.11,12 A test which can accurately identify which women will (or will not) experience a preterm birth would allow for targeted, appropriate and timely use of antenatal interventions including tocolytics, antenatal corticosteroids and magnesium sulfate, as well as referral and transfer of women to higher level facilities. This would optimize the benefits of these interventions, and minimize the possibility of harm. By avoiding unnecessary antenatal preterm interventions or hospital admissions, healthcare resource waste is reduced, as are any health risks associated with unnecessary medicine use.10

Biomarkers for Preterm Birth Prediction

There are few tools in clinical use for predicting which women presenting with preterm labour symptoms will experience preterm birth. Biomarkers have been identified as the most promising area for predictive tests. For example, the fetal fibronectin (fFN) test uses a vaginal swab to test fFN levels in cervicovaginal secretions of pregnant women.13 Though not currently recommended by WHO, some national and regional guidelines recommend fFN testing.14,15 fFN testing is one of the most common tools used for risk stratification of women presenting with symptoms of preterm birth, however it has faced challenges including inaccurate positive results, poor availability and limited manufacturing.13,16,17 As of September 2024, the sole manufacturer of rapid fFN testing cassettes has ceased production, resulting in worldwide shortages.17

Other biomarkers, such as placental alpha microglobulin-1 (PAMG-1) and a phosphorylated form of insulin-like growth factor binding protein-1 (phIGFBP-1), are used in commercially available tests but have not reached routine clinical care.18,19 Despite some advancements, existing biomarkers tests for preterm birth detection lack accuracy and affordability and are frequently unavailable due to limited manufacturing. In low- and middle-income countries, where health systems constraints and inequities in accessing care are common, these challenges are particularly problematic.

## Purpose of this Target Product Profile

Given the significant, wide-ranging, deleterious effects of preterm birth, accurate and accessible methods of predicting preterm birth in symptomatic women - such as with biomarker tests - are urgently needed.

Target Product Profiles (TPPs) are strategic documents designed to guide the development of new medical devices, diagnostics and drugs. TPPs outline the minimum and optimal desired product attributes, serving as a method to align key stakeholders on the characteristics a new product should have to meet its intended use. By setting a clear and structured roadmap to guide research and development (R&D) and regulatory processes, TPPs play a pivotal role in defining R&D priorities, identifying critical product attributes, and accelerating development of impactful health innovations.

Currently, no publicly available TPPs exist for biomarkers to predict preterm birth in women with symptoms of preterm labour. Given the significant global burden of preterm birth, and the promising nature of biomarkers for preterm birth prediction, the development of a TPP in this area is essential. This TPP will foster consensus on the minimum and optimal characteristics of preterm birth biomarker tests, guiding the development of affordable, accurate and accessible solutions.

# Summary: Intervention Use Case and Target Users

A biomarker test that can accurately predict if a pregnant woman with symptoms of preterm labour (e.g. contractions or cervical changes) will give birth within 14 days.

Such a test would permit accurate risk stratification and identify women at high risk of preterm birth. This would allow for antenatal interventions to improve preterm newborn outcomes to be used selectively and promptly. These interventions include tocolytics to delay preterm labour, antenatal corticosteroids for fetal lung maturation, magnesium sulfate for neuroprotection, and transportation of the woman to higher levels of healthcare services.

# Target Product Profile Variables

| **Variable** | **Minimum**  *The minimal target should be considered as a potential go/no go decision point.* | **Optimistic**  *The optimistic target should reflect what is needed to achieve broader, deeper, quicker global health impact.* | Annotations  *For all parameters, include here the source data used and rationale for why this feature is important.* |
| --- | --- | --- | --- |
| **Intended Use** | Biomarker test to accurately predict the likelihood of imminent preterm birth (within 2 weeks) in women with signs or symptoms of spontaneous preterm labour. | Same as minimum. | A prognostic test to identify women who will imminently give birth preterm allows for targeted and timely use of effective interventions to improve neonatal outcomes for preterm babies. WHO recommends tocolytics to slow labour, antenatal corticosteriods, magnesium sulfate, antibiotics, and (when relevant) transfer to higher level facilities.7-10 |
| **Target Population** | Pregnant women, adolescent girls, transgender and gender-diverse people presenting with signs or symptoms of spontaneous preterm labour, between 24- and 37-weeks’ gestational age. | Same as minimum. | Symptoms of spontaneous preterm labour can include uterine contractions, cervical dilation or effacement before 37 weeks' gestation.11 Interventions including tocolytics, antenatal corticosteroids and magnesium sulfate are recommended from 24 weeks’ gestation.7,9,10 |
| **Population unlikely to be treated** | Women presenting with intrauterine fetal death or with a clear indication for immediate delivery. | Same as minimum. | Women with a confirmed intrauterine fetal death should not be offered preterm labour testing. Women who have an indication for immediate delivery (e.g. severe preeclampsia) would also not benefit from testing. |
| **Target Countries** | All countries, including those with high rates of spontaneous preterm birth and related poor health outcomes. | Same as minimum. | Preterm birth occurs worldwide, with approximately 13.4 million babies born preterm globally.1 The majority of preterm births occur in low- and middle-income countries.1 |
| **Target End Users** | Skilled health personnel delivering antenatal care in health facilities.  Laboratory technician support may be required to run tests. | Any level of health worker, including community health workers.  No requirement for laboratory technician support. | Target end users refer to the individuals who will perform the biomarker test. The test should be simple enough for any relevant skilled health personnel (such as a doctor, midwife or nurse) to perform. If the test can be used and interpreted by community health workers, that would further widen access .20,21 Laboratory testing may be required, which would pose additional barriers to its use in limited-resource settings.22 |
| **Target Settings** | Primary, secondary and tertiary health facilities where women present for birth. | Any level of health facility where women present for birth, including community-based and mobile outreach settings. | The test should be designed for use across a range of healthcare settings to facilitate accessibility and impact. |
| **Tool Design and Functionality** | Simple test that may require laboratory processing. | Point-of-care test that does not require laboratory processing. | A simple test is essential to facilitate use by a range of healthcare cadres. Laboratory processing may be required but is not ideal. |
| **Sample Type** | Blood, cervicovaginal secretions, saliva or urine. | Same as minimum. | Where possible, tests samples that are minimally- or non-invasive, and do not require additional equipment (e.g. speculum examination) or specialist personnel, are preferred. |
| **Adjunct tests** | A standalone, single-parametric test. | Able to be incorporated into multiparametric tests or as a standalone test | A biomarker test may be performed as a standalone test, or be combined in a multi-parametric test (with or without an algorithm) to inform risk stratification. |
| **Test Result** | Clear qualitative or quantitative result. | Same as minimum. | The test should provide a clear qualitative result (e.g. positive or negative, detected or not detected) indicating presence of the relevant biomarker in the sample, or a quantitative result (e.g. a numerical reading) indicating the level of the relevant biomarker. |
| **Time to Result** | Results provided in ≤4 hours, including laboratory processing time. | Results provided in ≤30 minutes. | Point-of-care tests with quick results are preferred, especially in settings with limited healthcare access.23-25 Target times exclude sample collection. |
| **Sensitivity** | ≥90% | ≥99% | The sensitivity of a test refers to the ability of a test to truly detect those who have the disease. Fetal fibronectin testing has high sensitivity (100%) for birth within 7 days.27 Ideally, sensitivity of a novel test would be similar to existing prognostic tests. Prognostic data should be peer-reviewed and validated, ideally in different settings and populations. |
| **Specificity** | ≥70% | ≥85% | The specificity of a test refers to the ability of a test to truly detect those who do not have the disease. Test specificity should be equal to or better than existing prognostic tools. Fetal fibronectin testing has a specificity of 64% for birth within 7 days.27 Prognostic data should be peer-reviewed and validated, ideally in different settings and populations. |
| **Safety** | No adverse safety outcomes for pregnant women, neonates, or health personnel. | Same as minimum. | Use of the test should not pose any hazards to the patient or test user (i.e. health personnel), including hazards relating to blood/body fluid safety precautions. |
| **Training Requirements** | Less than one day of training required for skilled health personnel, including processing for laboratory technicians. | Less than one hour of training required for any level of health worker. | Clear, simple and contextually appropriate training is essential for proper test use. Where possible and necessary, training should be incorporated into broader training on prevention and management of preterm birth. |
| **Operational Requirements** | No more than five steps to retrieve sample and run test.  Maximum one timed step.  Additional steps may be required for laboratory processing of the sample. | No more than three steps to retrieve sample and run test.  No timed step. | Operation of the test should be as simple as possible for ease of use and duration required.  Timed steps and laboratory processing may be required but should be limited where possible. |
| **Operating Conditions** | Operational at 15-30°C and  40-70% humidity.  Cold chain may be required for samples. | Operational at 10-45°C and  40-90% humidity.  Cold chain not required. | Tests that require cold chain, either for storage or operation, are challenging to implement in many contexts. Some tests may require refrigeration of samples if not immediately processed.26 As such, it is strongly preferred that tests do not require cold chain. |
| **Stability and Shelf Life** | Stored for 12 months at up to 30°C, 70% humidity. | Stored for 24 months at up to 45°C, 90% humidity. | Tests should maintain stability in a range of storage temperatures to facilitate effective use globally. |
| **Reagents reconstitution** | All reagents ready to use. | Same as minimum. | For simplicity of use, reagents (substances that facilitate a reaction within the test) should not require reconstitution. |
| **Packaging and Labelling** | All test components included in one durable, easy to open package.  Instructions for use are printed on or with packaging, and are simple and pictorial.  Low environmental footprint. | Same as minimum. | Packaging of tests should facilitate efficient shipping and storage, reduce risk of damage, include clear instructions for use, and be easy to open.  Simple, pictorial instructions for use are particularly critical for community health workers with limited literacy.  Environmental footprint should be considered and limited where possible, to address environmental concerns. |
| **Waste Disposal** | Compatible with local biohazard waste disposal systems. | Compatible with local general waste disposal systems. | Test disposal must align with the medical waste disposal commonly used in local contexts. |
| **Regulatory and Quality Control** | Regulatory approval by relevant national authorities.  Meet relevant standards - ISO 13485:2016 (medical devices), ISO 15189:2022 (point-of-care tests) and ISO 20916:2019 (in vitro diagnostic medical devices). | Same as minimum.  Plus:  Approval by relevant international authorities. | Approval of the test is critical in the local contexts in which it is used. International approval can assist in accelerating scale up of implementation. |
| **Pricing** | ≤ USD $20 per test. | ≤ USD $1 per test. | An affordable test is essential, especially in lower-resource settings, to allow for widespread scale up. Price will vary across different manufacturers and countries. The costs stated do not include additional costs of laboratory processing equipment, if required.  The cost of fetal fibronectin, a current test for preterm birth prediction, ranges between countries. Available pricing data for fetal fibronectin ranges from USD 50 to USD 105 per test.28-31 |

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