Target Product Profile for Tools for measurement of postpartum blood loss after vaginal birth

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1. BACKGROUND

1.1 POSTPARTUM HAEMORRHAGE

Postpartum haemorrhage (PPH), characterized by excessive bleeding after childbirth, is a significant global health issue. An estimated 6% of women giving birth will experience PPH.[1] With approximately 70,000 associated maternal deaths annually, equivalent to over 20% of all maternal deaths, PPH is one of the largest contributors to maternal mortality globally.[2] While PPH can affect postpartum women in any context, those in low-resource settings are disproportionately affected - the highest rates of PPH and PPH-associated mortality are observed in sub-Saharan African and South Asian countries.[1,2] In addition to maternal mortality, PPH can result in a number of morbidities including hypovolemic shock, organ dysfunction, anemia and infection.[3-5]

The World Health Organization (WHO) defines primary PPH as 500 ml or more blood loss occurring within 24 hours postpartum, regardless of mode of birth.[2] Severe PPH is characterized by a blood loss exceeding 1000 ml.[6] Secondary PPH can occur up to 6 weeks following childbirth.[7] Clinical signs of excessive blood loss (including changes to blood pressure, heart rate, breathing and consciousness) are also important in PPH detection, however often present once substantial blood loss has already occurred.[8,9] PPH can occur after either vaginal or cesarean section births. It is most commonly caused by uterine atony, but can also be caused by lacerations, hematomas, uterine inversion, rupture, retained placental tissue, morbidly adherent placenta, or coagulopathy.[10] Furthermore, conditions such as anemia can significantly increase the risk of PPH.[11]

In 2023, WHO issued a new recommendation in favour of early PPH detection and using care bundles for treatment.[12] This care bundle should include multiple, effective interventions - uterine massage, administration of an oxytocic agent and tranexamic acid, intravenous fluids, examination of the genital tract and escalation of care.[12] However, prompt initiation of these interventions relies upon early and accurate detection of PPH. Consequently, WHO also recommended routine, objective measurement of blood loss for all postpartum women, in order to facilitate timely identification and treatment of PPH.[12] Blood loss measurement should commence from the delivery of the baby and continue as long as active bleeding persists, or if the woman remains unstable after PPH.[13] Failure to accurately measure postpartum blood loss, alongside recognizing relevant clinical signs, will likely translate into delays in detecting PPH and commencing effective treatments – these delays can be life-threatening to the woman.

There are a number of different approaches used for estimation or measurement of blood loss and detection of PPH. Currently, subjective visual assessment of blood loss is widely practiced, which has proven to be unreliable. For example, visual estimation of blood loss often leads to overestimation when blood loss volume is low, and underestimation when blood loss volume is high.[14-16] Other, more objective methods aim to quantitate the amount of blood loss, such as the use of gravimetric techniques (collecting and weighing) or uncalibrated drapes.[17,18] More recently, single use calibrated drapes have been shown to be accurate for postpartum blood loss measurement.[19,20] In a recent multi-country trial (E-MOTIVE trial) calibrated drapes were used to enable prompt identification of PPH in women giving birth vaginally.[21] However, environmental concerns and cost implications of single use products are stimulating design of innovative reusable tools.[22] More complex technologies such as measuring haemoglobin (Hb) concentration in venous blood samples using spectrophotometry can also measure postpartum blood loss.[19] However, implementation of these technologies can be challenging and time consuming, particularly in resource-constrained settings.[16]

WHO has acknowledged the lack of advancement in PPH knowledge and technologies throughout the past decade, necessitating the development of innovative diagnostic strategies.[2] While several blood loss measurement tools exist, there is yet to be global scale up of accurate, user-friendly and affordable tools for this purpose. This contributes to delays in identifying PPH and missed opportunities to implement effective treatment interventions that could prevent PPH-related morbidity and mortality. Given the significant impact of PPH on maternal health outcomes, particularly in low- and middle-income countries (LMICs), there is a pressing need for accurate, accessible, sustainable and affordable methods to be available, wherever women give birth.

1.2 PURPOSE OF THIS TARGET PRODUCT PROFILE

Target Product Profiles (TPPs) are strategic documents that outline the minimum and optimal characteristics required for new health products, including devices and medicines. TPPs are an important resource to guide key stakeholders (such as funders, researchers, product developers, manufacturers and regulators) on the requirements of new medicines, diagnostics and devices to meet pre-specified clinical and public health needs.[23] They inform research and development strategies, help frame product dossiers, streamline communication with regulatory agencies and help funders set targets.[24]

There are currently no TPPs publicly available for PPH blood loss measurement devices.[25] WHO have identified the need for TPPs for PPH interventions to create a shared understanding on ideal characteristics of innovative PPH products.[2] Development of this TPP is intended to help drive innovation, research and implementation of effective and affordable devices that can accurately measure postpartum blood loss, particularly in low-resource settings. This will improve the timely detection of PPH, allowing for implementation of PPH care bundles as clinically necessary.

2. SUMMARY: INTERVENTION USE CASE

A tool that can measure postpartum blood loss and aid in the detection of primary PPH for vaginal births, from the third stage of labour up to 24 hours after birth. It will provide an objective measurement of real-time blood loss, rather than a subjective visual estimate, to ensure accuracy. A user-friendly, women-friendly and inexpensive design will ensure it is a simple and effective tool that is suitable for use across all healthcare facilities globally, including in limited-resource settings. By enabling timely and accurate blood loss measurement, this tool will optimise use of and adherence to treatment protocols for PPH.

3. TARGET PRODUCT PROFILE

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 / Actual Product Performance[1] *For all parameters, include here the **source data used and rationale** for why this feature is important.*
Indication	Accurate measurement of blood loss and detection of PPH from the third stage of labour until at least 1 hour after vaginal birth.	Accurate measurement of blood loss and detection of PPH from the third stage of labour up to 24 hours (as necessary) after vaginal birth.	In order to ensure accuracy of blood loss amounts, objective quantification should be used rather than subjective estimations, such as visual estimation.[14-16] Large trials have measured blood loss over the first hour postpartum.[21] However, primary PPH can occur up to 24 hours after birth, including once women have left the delivery suite. The time period of blood loss measurement should balance clinical necessity and acceptability to the woman. While PPH can also occur during caesarean section births, blood loss measurement tools will have different requirements compared to vaginal births, so are not included in this TPP.
Target Population	All pregnant women, girls, trans and gender-diverse people who are giving birth vaginally.	Same as minimum.	Postpartum blood loss and PPH can affect any person giving birth. While some risk factors for PPH are known, it is difficult to accurately predict which women are at higher risk of PPH.[26] Because of these challenges in predicting PPH, blood loss measurement should be utilised for all women giving birth. Tools may also be

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			used to measure vaginal bleeding following caesarean deliveries.
Target Countries	All countries, including limited-resource settings and countries with the highest burden of PPH.	Same as minimum.	PPH can occur in any country. Therefore, accurate measurement of postpartum blood loss is an important intervention globally. Rates of PPH and associated maternal mortality are highest in regions including sub-Saharan Africa and South Asia.[2] Blood loss measurement tools must be suitable for use in all contexts.
Target Users and Settings	Skilled health personnel providing intrapartum care and immediate postpartum care. Suitable for use in different levels of healthcare facilities (primary, secondary and tertiary).	Same as minimum. Plus: Suitable for use in home-or community-based settings where birth is attended by skilled health personnel. Suitable for use during emergency patient transfers.	The healthcare cadre responsible for using tools to measure postpartum blood loss may differ between countries, settings and health facilities. For example, this could include midwives, nurses, obstetricians, or community health workers (CHWs).[19,27-30] As such, the tool must be simple enough for relevant skilled health personnel to use. Blood loss measurement tools may also be used for home births, in community health facility settings, and for patient transfers by ambulance to or between health facilities.
Tool Design	Single use or reusable.	Same as minimum. Plus:	Whether tools are single- or multi-use can have impacts on cost-effectiveness, patient safety, cleaning requirements and environmental sustainability. Single-use or reusable tools will likely be preferred in different settings.

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		Able to be used in multiple birth and postpartum positions.	There are various birthing positions that women may choose during birth.[31] As such, it is necessary to have tools that can measure blood loss in different birth positions.
Output and display of blood loss volume	Volume of blood loss able to be clearly and quickly determined. Produces a reliable, consistent, standardised and accurate measurement of blood loss volume. Calibrated with indicators showing volume of blood. Clinically significant thresholds of blood volume clearly marked to trigger detection, treatment and escalation of PPH.	Same as minimum. Plus: No additional equipment or specific technical expertise required to read results. Digital or non-digital features for recording and/or documenting blood loss volume measurements to assist in clinical documentation may be included.	Tools that clearly show volume of blood loss are necessary for accurate measurement. Having indicators at certain blood loss volumes to trigger closer monitoring of other signs of blood loss and prepare to deliver interventions to treat PPH, facilitates more effective prevention and treatment of PPH-related mortality and morbidity. For example, calibrated drapes used in the E-MOTIVE trial had indicators at 300 ml and 500 ml.[21] If the device measures and notifies the care provider when a certain threshold is exceeded that may be an advantage. The readings should not be dependent on the position or shape of the device. Accurate blood volume readings should not require intervention such as manual sweeping of pooled blood into a collection tool.
Time to result	Real time, immediate results.	Same as minimum.	Accurate measurement of blood loss in real time is essential to monitor blood loss as it occurs.[32] This also

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			facilitates ongoing, cumulative blood loss measurement. In doing so, the rapid assessment of blood loss will facilitate timely detection of PPH and trigger treatment interventions. Tools (such as laboratory tests) that do not have real time results, but rather require a period of waiting time before reading results, would lead to a delay in detection of PPH.
Training Requirements	Simple training suitable for any level of skilled health personnel, with options for in-person, remote, video-based or simulation training. Simple instructions for use provided with tool.	Same as minimum.	Tools should be simple to use and not require extensive training. Any skilled health personnel, with any level of training or qualification (including CHWs) should be able to effectively use the tool.
Instrument service and maintenance	For single use tool, none required. For reusable tool, easily and safely able to be cleaned.	Same as minimum.	Tool should not require servicing or maintenance if a single use product. No highly technical equipment or parts requiring specialist expertise to set up or maintain. For reusable products, it is critical that reprocessing (i.e. cleaning) of products is simple, safe and effective.[33] This must be achievable with easily accessible and affordable cleaning products.
Blood Volume Containment	Accurate measurement of blood volume lost within +/- 50mL. Able to contain at least two liters of blood.	Accurate measurement of blood volume lost within +/- 25mL. Able to contain at least two liters of blood.	Blood loss measurement tools should have calibrations and/or thresholds that accurately show the true amount of blood collected.

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Complexity	Set up in <3 steps. Requires one person to set up and use.	Set up in 1 step. Requires one person to set up. Automated alerts remove need for manual checking of blood volume.	The tool should be as simple as possible to unpack, set up, and use. Regardless of which cadre is utilizing the device, it should be possible to set up and implement and read results by one person. In many settings, women give birth with only one skilled health personnel present, so complexity of the tool must allow for this situation.
Safety	Safe for use by all women delivering vaginally, neonates, and skilled health personnel.	Same as minimum.	There should be no safety concerns associated with use of the tool, including minimizing risk of infection, allergies or skin irritation, or leakage/spillage and slips or falls. Safe and easy disposal of the tool and contained blood is critical.
Environmental Stability and Impact	Able to be transported and stored in a wide range of climatic conditions, including high humidity, dust and heat. 3-5 year shelf life in climatic zone IVb (simulated with 30°C and 75% relative humidity).	Same as minimum. Plus: Suitable for use at all temperature and humidity levels. *For single use:* Sustainable or biodegradable materials, and climate-friendly tool. *For reusable: Easy* to clean and re-use.	In order to be implemented globally, the tool must be suitable in all climate conditions, without affecting the quality or performance of the product. Consideration should be given to reducing environmental impact of the tool, including through design, manufacturing and disposal.

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Regulation and Quality Management	Approval by relevant national authority.	Approval by relevant national authority and at least one international stringent regulatory authority. Quality certification through an international organization.	Blood loss measurement tools should be approved for use by the relevant national authority (e.g. government health department or administration) in the country of intended use.[35] Additionally, approval from internationally recognised regulatory authorities may streamline implementation roll-out. Certification, such as ISO 13485 for medical devices can help to ensure high quality and safety standards are met.[36]
Women's Experience	Design and functionality of the tool considers the experience and comfort of women.	Same as minimum.	Women-centered care is essential for a positive birth experience.[34] As such, design and use of the tool must ensure respect, comfort and dignity for women giving birth. Privacy and cultural considerations are also important factors for acceptability.
Packaging	Easily packable.	Same as minimum. Plus: Minimal environmental footprint with recyclable packaging.	Devices should be easy to pack to ensure efficiency throughout the supply chain, with mitigation of any damage to devices during transit. Packaging should consider weight, size and storage. Where possible, consideration should be given to the potential environmental impacts of medical devices.
Price	Affordable for use in low-resource settings, while maintaining high quality.	Same as minimum. Plus:	Blood loss measurement tools must be low-cost and affordable to facilitate wide-spread use, particularly in

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		Unit cost is less than existing tools for objective blood loss measurement. Discounts for bulk procurement available for governments, international health agencies, and large health facilities. Able to be manufactured locally or regionally, with guaranteed quality assurance, to reduce costs.	limited-resource settings. The expected price of single use compared to reusable tools will differ. Where possible, costs should be less than existing tools for the same indication and pose no cost barriers to women. For example, calibrated drapes can currently be purchased for approximately USD 1.25.[37] Reusable tools may be more expensive but should have a low cost-per-use. Strategies to keep costs low, such as bulk procurement discounts and local manufacturing, may support in increasing the accessibility and availability of blood loss measurement tools.[38]
Procurement Estimates	Procurement quantity compatible with global or regional rate of vaginal births.	Same as minimum.	Approximately 134 million births occur each year.[39] An estimated 21% of births globally are caesarean sections, therefore an estimated 105 million vaginal birth occur each year.[40] However, the rates of caesarean section compared to vaginal births differ greatly among different countries.[41] Fewer blood loss measurement tools will be required if they are reusable compared to single use. Tools may be integrated into safe birth kits.

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