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NEST360°

Target Product Profile

Bilirubinometer – Jaundice Management

1ST EDITION, MARCH 2020

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Acknowledgements
This report was prepared by Rebecca Kirby and Kara Palamountain from Northwestern University with input from UNICEF and other stakeholders. The document summarizes consensus achieved at a meeting on target product profiles for newborn care in low-resource settings, convened by NEST360°. This document was finalized following consideration of all comments and suggestions made by meeting participants at the Consensus Meeting.

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Note to the reader
Because of the richness of the discussion, and in an attempt to keep this report simple and readable, this report aims to convey the themes addressed in each session, rather than attempting to provide a chronological summary of the dialogue.

Disclaimer: The TPPs do not replace or supersede any existing UNICEF TPPs. The TPPs do not constitute tender specifications, nor is UNICEF bound to tender or procure products that arise as a result of these TPPs. UNICEF may require regulatory approval and proof of compliance to quality management and product-specific international standards for tendering purposes.

INTRODUCTION

Most neonates, term and preterm, will have elevated levels of unconjugated bilirubin and some amount of jaundice during the first one to two weeks of life due to increased levels of unconjugated bilirubin with transient impaired excretion, which is normal in this age group. This condition is particularly prevalent in preterm babies and, if the levels of unconjugated bilirubin are very high and left untreated, may lead to irreversible neurologic damage known as kernicterus.

Phototherapy treats unconjugated hyperbilirubinemia that exceeds safe levels. These levels are based on day of life and risk factors and typically occur within the first one to two weeks of life.

Treatment with blue light phototherapy is necessary to prevent morbidity and mortality from dangerous levels of neonatal jaundice. The blue light is absorbed by bilirubin, which is then broken down in the blood, allowing the infant to excrete the excess bilirubin before it can accumulate and cause permanent brain damage (kernicterus) or death. Jaundice is preventable and treatable; however, kernicterus is permanent and irreversible, resulting in life-long disability.

Severe jaundice may not be readily evident to the naked eye until already at dangerously high levels. Additionally, jaundice may not present until several days after birth when an infant has already left the hospital. Thus, early monitoring of bilirubin in at-risk infants is critical in order to prevent severe jaundice, which may result in permanent neurological damage, particularly in premature babies who are at greater risk of death and disability due to jaundice.

All infants should have a laboratory evaluation of serum bilirubin (with result turn around within six hours) both to diagnose jaundice and to guide treatment of infants receiving phototherapy. In low-resource settings though, many facilities do not have the ability to run a blood test, and those that do face many challenges both to run the test and obtain results within a meaningful timeframe.

The ideal solution in a low-resource setting would be a reliable point-of-care test which can test serum bilirubin both before and during phototherapy treatment.

DEVELOPING A TARGET PRODUCT PROFILE

Overview

Manufacturers need Target Product Profiles (TPPs) at an early stage in the medical device and diagnostic development process. These TPPs help inform the ideal targets and specifications and align with the needs of end users. TPPs outline the most important performance and operational characteristics as well as pricing. In the TPPs to follow, the term "Minimal" is used to refer to the lowest acceptable output for a characteristic and "Optimal" is used to refer to the ideal target for a characteristic. The Optimal and Minimal characteristics define a range. Products should meet at least all of the Minimal characteristics and preferably as many of the Optimal characteristics as possible. TPPs should also specify the goal to be met (e.g. to initiate treatment), the target population, the level of implementation in the healthcare system and the intended end users.

For the NEST360° Newborn Care in Low-Resource Settings Target Product Profiles, an initial set of TPPs were developed listing a proposed set of performance and operational characteristics for 16 product categories. The development timeline envisioned in the TPPs was four years, although some commercially available technologies may fit some of the criteria already. For several of the characteristics, only limited evidence was available and further expert advice was sought from additional stakeholders.

Delphi-Like Process

To obtain this expert advice and to further develop the TPPs, a Delphi-like process was used to facilitate consensus building among stakeholders. The initial TPPs were sent to a more comprehensive set of stakeholders including clinicians, implementers, representatives from Ministry of Health, advocacy organizations, international agencies, academic and technical researchers and members of industry. In total, 103 stakeholders from 22 countries participated in the TPP development process via survey.

13 respondents participated in the Delphi-like survey for the Bilirubinometer.

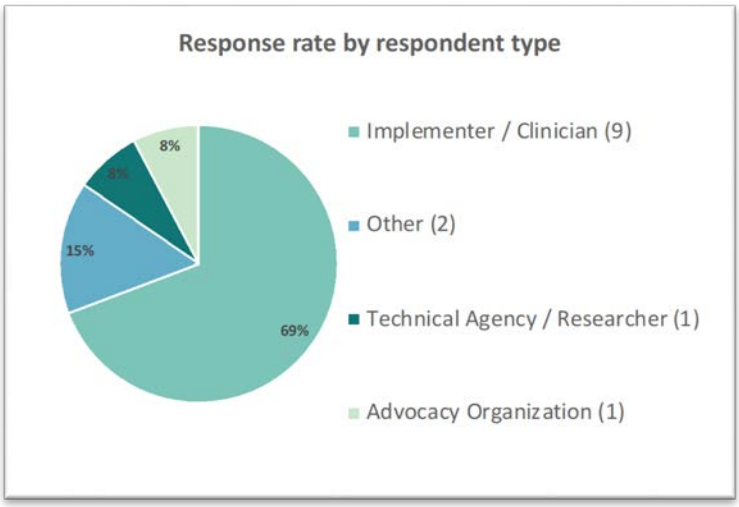
Survey respondents were requested to provide a statement on their level of agreement with each of the proposed characteristics for each TPP. Agreement was scored on a Likert scale ranging from 1 to 5 (1=disagree, 2=mostly disagree, 3= neither agree nor disagree, 4=mostly agree, 5=fully agree) with an option to opt out with the selection of "Other - Do not have the expertise to comment". If participants did not agree with the characteristic (i.e., selected 3 or below) they were asked to provide an explanation with comments. Participants who agreed with the statements could also provide comments however were not explicitly asked. In total, over 1,780 comments were reviewed and summarized in this report.

For each characteristic in each product category, a percentage agreement was calculated for both the Minimal and Optimal requirements. The percentage agreement was calculated as the ratio of the sum of number of respondents who selected 4 and 5, to the sum of numbers of respondents who gave any score (from 1 to 5 where 5=fully agree, 4=mostly agree, 3=neither agree nor disagree, 2=mostly disagree and 1=disagree). Consensus for the survey characteristics was pre-specified at greater than 50% of respondents providing a score of at least 4 on the Likert scale.

A classic Delphi process requires at least two rounds of survey ahead of an in-person meeting. Initially, two rounds of the survey were planned, but since 50% consensus for most characteristics was reached after the first round survey, a second round survey was not initiated. Survey results are detailed by characteristic in the individual product category sections.

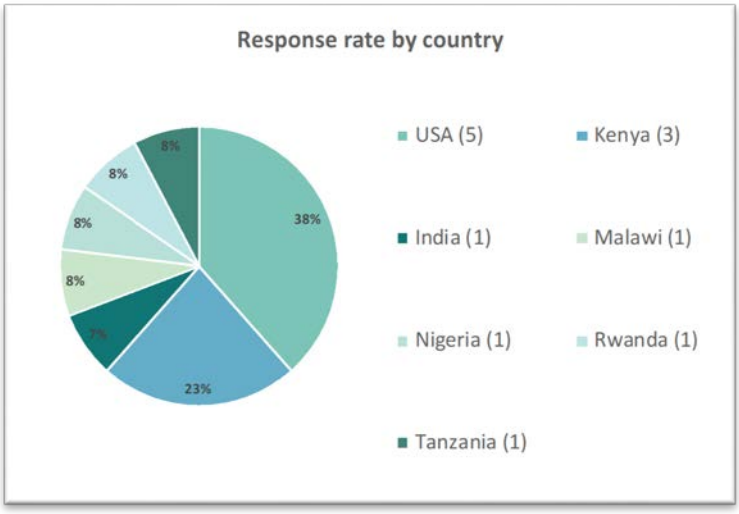
In total, over 180 organizations/individuals were asked to participate in this Delphi-like survey process, of whom 103 (see Appendix A) responded (response rate, 56%). Survey respondents were asked to self-disclose their affiliation.

Figure 1: Summary of organizational affiliation for Bilirubinometer TPP from Delphi-like Survey prior to Consensus Meeting (data as of Oct 25, 2019)



Respondent type	Percentage
Implementer / Clinician (9)	69%
Other (2)	15%
Technical Agency / Researcher (1)	8%
Advocacy Organization (1)	8%

Figure 2: Summary of response rate by country for Bilirubinometer TPP from Delphi-like Survey prior to Consensus Meeting (data as of Oct 25, 2019)



Country	Percentage
USA (5)	38%
Kenya (3)	23%
India (1)	8%
Malawi (1)	8%
Nigeria (1)	8%
Rwanda (1)	8%
Tanzania (1)	8%

Consensus Meeting

On November 20 - 22, 2019 over 69 stakeholders gathered in Stellenbosch, South Africa to focus on building further consensus on areas of discrepancy in opinion within the 16 TPPs. More specifically, characteristics on which fewer than 75% of the respondents agreed, or on which a distinct subgroup disagreed, were discussed. Consensus Meeting moderators presented the results and comments from characteristics with <75% agreement from the Delphi-like survey, the moderators then solicited additional feedback on each characteristic with <75% agreement from the Consensus Meeting participants, and then a proposed change to the TPP characteristic was discussed amongst Consensus Meeting participants. In some cases, Consensus Meeting participants nearly universally agreed on proposed changes. In other cases, Consensus Meeting participants failed to reach 75% consensus on proposed changes. If consensus was not achieved after two votes on proposed changes, meeting participants agreed to move forward and the disagreement is noted in this report.

Methodology for Mentimeter Voting Results: Certain proposed changes to TPP characteristics, for which a distinct subgroup disagreed, were anonymously voted on using Mentimeter.com to determine the overall level of agreement and disagreement amongst the Consensus Meeting participants. The Mentimeter Voting Results are presented throughout this report in three distinct categories:

I. Overall vote – Includes all Consensus Meeting participants who voted on Mentimeter.com. To eliminate the possibility of duplicate votes, all respondents were asked to enter their name (to be viewed only by the report authors) and blank (potentially duplicate votes) were eliminated from the overall vote.
II. Clinicians – Includes all Consensus Meeting participants who voted on Mentimeter.com and who designated themselves as a Clinician on Mentimeter.com.
III. Excluding involvement with product development - Includes all Consensus Meeting participants who voted on Mentimeter.com minus those who indicated on a Declaration of Interest form that they are 'currently or have been involved in the development of a candidate technology or product' specific to the Product Category being voted on.

Of the 133 stakeholders that were invited to the meeting, 69 participants were able to attend. Participants comprised country representatives, stakeholders from technical and funding agencies, researchers, implementers and civil society organizations, and representatives from companies working on newborn care technologies (see Appendix B for the Consensus Meeting Participant List). An overview of the discussion for Bilirubinometer and final consensus achieved is included in this report. Most characteristics discussed are presented in this report, however, overarching characteristics that applied to all product categories were discussed in unison and are included in the NEST360° Newborn Care in Low-Resource Settings Target Product Profiles. These characteristics are: Target Operator; Target Population; Target Setting; Quality Management; Regulation; User Manual/Instructions; Warranty; Power Source; Battery; Voltage; Power Consumption.

FINAL TPP - BILIRUBINOMETER

Final target product profile for Bilirubinometer		
Characteristic	**Optimal**	**Minimal**
SCOPE		
Intended Use	Quantification of serum bilirubin in neonates for the diagnosis and management of jaundice at the patient's bedside	
Target Operator	For use in low- and middle-income countries by a wide variety of clinicians, including nurses, clinical officers, and pediatricians	
Target Population	Neonates (born at any gestational age and require ongoing care)	
Target Setting	Hospitals in low-resource settings	
SAFETY AND STANDARDS		
Quality Management [1]	ISO 13485:2016 Medical devices – Quality management systems -- Requirements for regulatory purposes	
Regulation	At least one of: CE marking, approved by US FDA or another stringent regulatory body of a founding member of IMDRF (e.g., Japan or Australia or Canada)	
TECHNICAL CHARACTERISTICS		
Linear Range	0-40 mg/dL (0-684 µmol/L)	5-30 mg/dL (85.5 - 513 µmol/L)
Accuracy	± 10% from 5-30mg/dL (85.5 - 513 µmol/L)	± 20% from 5-30mg/dL (85.5 - 513 µmol/L) [2]
Results Format	Quantitative across whole linear range	
Result Units	Must display mg/dL or µmol/L (shall have ability to select or switch between either)	
Precision	4% CV	15% CV
Sample	Whole blood heel-stick sample <50 µL; does not require user to separate serum/plasma using a centrifuge	
Calibration	No calibration	Minimal user calibration required
Kit Stability & Storage	Stable for >12 months with harsh ambient conditions (temperature 5-45 °C, humidity 15% to 95%, dusty air, elevation >=2000 meters) and transport stress (48h with fluctuations up to 50°C and down to 0°C)	Stable for 12 months with harsh ambient conditions (temperature 10-40 °C, humidity 15%-95% elevation up to 2000 meters) and transport stress (48h with fluctuations up to 50°C and down to 0°C)
Equipment Required	Small, portable or hand-held device; device-free/disposable preferred; does not require centrifuge	Small, table-top device; portable device optional; does not require centrifuge
PURCHASING CONSIDERATIONS		
Instrument Pricing	<$200 ex-works	<$800 ex-works
Consumable Pricing	<$0.50 per test ex-works	$1.50 per test ex-works

UTILITY REQUIREMENTS		
Power Source	No power required	Mains with rechargeable battery
Battery	None (i.e. a disposable test that requires no electricity)	Rechargeable battery, >100 tests on a single charge.
Voltage	None.	Model must match the voltage and frequency of the purchasing country's local power grid (e.g., 110-120 VAC at 60 Hz or 220-240 VAC at 50 Hz)

[1] *There was not 75% voting agreement on the Minimal characteristic. Please refer to the TPP Report discussion for additional detail.*
[2] *Source: https://www.westgard.com/2019-clia-changes.htm CLIA proposed changes define Accuracy as ±20%. These changes are proposed as of Feb 2019.*

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Consensus Meeting Summary: Bilirubinometer

To arrive at the final TPP for Bilirubinometer, we conducted a pre-meeting survey to prioritize the items for discussion at the Consensus Meeting for characteristics that achieved below 75% agreement in the survey results. An overview of the discussion at the Consensus Meeting of these characteristics is included below.

- **Linear Range**
  - Consensus was achieved in the room (without a Mentimeter vote) for the Minimal characteristic. Clinicians noted that the upper end of the range was more important (since above roughly 25mg/dL will not change behavior) and that 5mg/dL for the lower end of the range was acceptable. From a technical perspective, product developers noted that going above 25mg/dL was relatively easy up to 30mg/dL, especially compared to extending the lower end of the range. Product developers explained that reducing the lower end was more expensive, but 3-4mg/dL detection was reasonable from a manufacturing perspective.
  - *Minimal: 5 - 30 mg/dL* (85.5 - 513 µmol/L)
- **Accuracy**
  - Consensus was achieved in the room (without a Mentimeter vote) for both the Optimal and Minimal characteristics. Participants noted new proposed CLIA laboratory standards [1]. Clinicians mentioned that central laboratory results take more time in low-resource settings (often a minimum of 24 hours). Since clinicians may rely on quick turnaround point-of-care tests in low-resource settings, clinicians requested better accuracy at higher ends of the range, hence the decision to be more stringent than the proposed CLIA standards for the Optimal characteristic. Clinicians noted that at the high and low ranges though, their behavior for treatment would likely not change. Product developers noted that it is a "big ask" to improve beyond 10% accuracy as a centrifuge and other lab equipment for blood sample testing would be required.
  - *Optimal: ±10% from 5-30mg/dL (85.5 - 513 µmol/L)*
  - *Minimal: ±20% from 5-30mg/dL (85.5 - 513 µmol/L)*
- **Results Format**
  - Consensus was achieved in the room (without a Mentimeter vote) for the Minimal characteristic to equal the previously agreed upon Optimal characteristic.
  - *Optimal: Quantitative across whole linear range.*
  - *Minimal: Same as Optimal.*
- **Results Unit**

- Consensus was achieved in the room (without a Mentimeter vote) for both the Optimal and Minimal characteristics.
- *Optimal: Must display mg/dL or µmol/L (shall have ability to select or switch between either)*
- *Minimal: Same as Optimal.*

- **Instrument Pricing**
  - Consensus was achieved in the room (without a Mentimeter vote) to keep the Minimal characteristic under $800 ex-works and emphasize the disagreement in the room on setting a reasonable price. Participants highlighted that the cheaper the price the better, however, noted the clear tradeoff between instrument and consumable pricing (i.e., if consumables were cheap at $0.05 per test, then $800 could be acceptable). Since there are not many benchmarks on the market, the price point for what this would cost is not clear. One research question for the future would be to evaluate the number of false positives and false negatives based on clinical diagnosis data versus a point-of-care tool. The outcome of this comparison, may be used to justify the purchase of the point-of-care tool.
  - *Minimal: <$800 ex-works*
- **Number of steps**
  - Consensus was achieved in the room (without a Mentimeter vote) that the fewer steps the better and therefore, it was suggested that this characteristic be removed from the TPP since there was variation in measurement of the number of steps.

Broad Themes and Considerations

At the Consensus Meeting, the following additional themes emerged and are summarized below:

Instrument Pricing

In order to provide a consistent measure of pricing, the ex-works price is included in the TPPs. Participants highlighted that ex-works pricing is not a true measure of landed cost and is often vastly understated to what a procurement agent will pay. One participant from an international NGO noted that there is a "minimum 30% mark-up on the ex-works price." The rationale for using the ex-works price is that it is a reliable measure that can be used for consistent comparison across geographies since distributor markups vary by country and geography.

Utility Requirements

A significant portion of the discussion was devoted to deliberating on how equipment can be designed to work in health facilities with limited electrical infrastructure. Designing the equipment for low-resource conditions often requires back-up batteries which adds to the expense of the technology, as well as the size of the equipment which can pose a challenge in crowded newborn wards. Some participants noted that rather than designing equipment for these facilities with limited electrical infrastructure, to consider whether a broader investment in electrical infrastructure would be a better use of funds. This inherent tradeoff was discussed multiple times when electrical characteristics were discussed.

Additionally, there were a variety of characteristics in the initial survey that related to Utility Requirements (i.e., electricity and power) that varied slightly in title across the TPPs. During the TPP Consensus Meeting, participants agreed that all characteristics relating to Utility Requirements (includes Back-up Battery; Battery Power; Batteries; Voltage; Power Requirement; Maximum Power Consumption; Response During Power Outage; Surge Protection, Electrical Plug) be reviewed and harmonized following the TPP meeting across the product categories. These characteristics have since been reviewed and harmonized into four distinct characteristics (Power Source, Battery, Voltage, and Power Consumption) in the final TPPs.

- **Power Source** - This defines the desired power source for the device and can be broken down into the following categories:

- *Mains power* - device must be plugged into a mains power source for use
- *Mains with battery backup* - device must be plugged into a mains power source for use, however, in the case of a power failure, the device has a battery backup that can last a specified period of time
- *Mains with rechargeable battery* - device has a rechargeable battery that operates both when the device is charged by a mains power source, or, when the device is plugged in (e.g., a mobile phone)
- *Battery is disposable and replaceable*
- *No power required (i.e., disposable device)*

- **Battery** - This includes the length of time the rechargeable or disposable battery should function
- **Voltage** - This specifies the preferred voltage conversion if the Power Source utilizes Mains Power. Note that for certain technologies (i.e., Bilirubinometer, Glucometer, Hemoglobinometer, pH monitor, and Pulse Oximeter), the Voltage characteristic is included in reference to the rechargeable battery charger requirements. For example, while the Optimal Voltage characteristic is "None" (i.e., no charging is necessary), the Minimal Voltage characteristic should conform to "the voltage and frequency of the purchasing country's local power grid (e.g., 110-120 VAC at 60 Hz or 220-240 VAC at 50 Hz)" to ensure that the charger for the battery is compliant.
- **Power Consumption** - This specifies the maximum Watts of electricity that the device should consume

Ideally, all devices should be developed to withstand power surges and voltage spikes.

Note that comments received in the Pre-Meeting survey report highlighted the importance of the correct frequency in electrical plugs. It was noted that a universal adaptor would not safely support the conversion of 60Hz equipment to 50Hz and that a machine relying on this method could fail in a short period of time (applicable to Oxygen Concentrator, Warming Crib, Radiant Warmer).

Delphi-like Survey: Bilirubinometer

Delphi-like survey results for Bilirubinometer TPP prior to Consensus Meeting (data as of Oct 25, 2019)

	Optimal		Minimal		
Characteristic	**Optimal requirement**	**% agreement (n size)**	**Minimal requirement**	**% agreement (n size)**	**Collated comments from Delphi-like survey**
Intended Use	Optimal: Quantification of total serum bilirubin in neonates for the diagnosis and management of jaundice at the patient's bedside	**92% n = 13**	Minimal: Same as Optimal.	**100% n = 12**	1 comment • Ideally, would pair together the ability to simultaneously test for Coombs positivity and bilirubin on the same POC machine • I would also say Optimally this would report direct and indirect separately (would diversify its utility to other parts of the hospital outside of neonates)"
Target Operator	Optimal: For use in low- and middle-income countries by a wide variety of clinicians, including nurses, clinical officers, and pediatricians.	**100% n = 13**	Minimal: Same as Optimal	**100% n = 12**	0 comments

	Optimal		Minimal		
Target Population	Optimal: Neonates (<28 days)	**85%** **n = 13**	Minimal: Same as Optimal.	**100%** **n = 11**	4 comments as summarized below Theme: Broaden age range • Sometimes you have babies that are > 28 days. e.g., 40 days would be ideal • Optimally this could be used in older people as well, not sure if fetal hemoglobin is affecting how this test works or not
Target Setting	Optimal: Hospitals in low-resource settings	**83%** **n = 12**	Minimal: Same as Optimal.	**91%** **n = 11**	2 comments as summarized below Theme: Broaden Target Setting • Potentially higher income countries • The jaundiced babies will be referred from lower level facilities; health centers and this test should be available from those lower level facilities up to hospitals so as to benefit all the at-risk babies • Minimal: hospital in resource-limited settings, Optimal: health centers (primary)
International Standard	Optimal: ISO 13485:2016 Medical devices – Quality management systems -- Requirements for regulatory purposes.	**100%** **n = 7**	Minimal: Same as Optimal.	**100%** **n = 6**	0 comments
Regulation	Optimal: CE marking or US FDA Clearance	**89%** **n = 9**	Minimal: Same as Optimal.	**88%** **n = 8**	1 comment as summarized below • Consider additional 'or' options: o Other Stringent Regulatory Authorities – Japan or Australia or Canada o Consider regulatory bodies of Low- and Middle-Income Countries
Linear Range	Optimal: 0-40 mg/dL	**91%** **n = 11**	Minimal: 0-30 mg/dL	**64%** **n = 11**	6 comments as summarized below Theme: A variety of ranges were suggested • Minimal would be 5-25 (these are the clinically meaningful numbers for intervention in terms of both phototherapy and exchange transfusion. Having accuracy outside of this window may interest people for research reasons? But won't change clinical management that I'm aware of • Minimal is still too high – should be more like 20 • As long as minimal has high reading for >30

	Optimal		Minimal		
Accuracy	Optimal: Within 20% or 0.4 mg/dL, whichever is greater	**69%** **n = 13**	Minimal: Same as Optimal.	**55%** **n = 11**	7 comments as summarized below Theme: Accuracy definition needs clarity. A range of perspectives were provided. • "Needs to be whichever is lower, 20% or .4 mg/dL" • "Given that the range in which most clinically meaningful bilirubin decisions would be made (5-25mg/dL) +/- 20% seems too generous? +/- 1mg/dL serum bili seems more reasonable to me" • "Need more accuracy • Recommend changing minimal to within 25% or 2mg/dL" • "0.4mg/dL is reasonable. However 20% would not be acceptable in higher values. For example of the bilirubin level is 20 mg/dL and the accuracy ranges from 18-22mg/dL, that could alter management decisions if it were 18 or 22. 20% or 0.4mg/dL whichever is lower would be more appropriate."
Results Format	Optimal: Quantitative across whole linear range	**100%** **n = 13**	Minimal: Quantitative; semi quantitative below 2 or above 20 mg/dL	**67%** **n = 12**	3 comments as summarized below Theme: Minimal should require quantitative across the whole linear range
Result Units	Optimal: mg/dL and mmol/L	**92%** **n = 12**	Minimal: Same as Optimal.	**64%** **n = 11**	5 comments as summarized below Theme: Variation in unit defined in guidelines across countries • "We are used to mmol/L but international guidelines use mg/dL" • "mmol/L because our guidelines are written mmol/L" • "Most tables are labeled with both so I think reporting in one or the other is also fine" • "Easy to change" • "Minimal might be. 'mg/dL or mmol/L' set at factory pre-shipment'"
Precision	Optimal: 4% CV	**88%** **n = 8**	Minimal: 15% CV	**86%** **n = 7**	3 comments as summarized below Theme: Precision / CV is not an understood term / unit
Sample	Optimal: whole blood heel-stick sample <50 µL; does not require user to separate serum/plasma using a centrifuge	**100%** **n = 11**	Minimal: Same as Optimal.	**100%** **n = 10**	4 comments as summarized below Theme: Questions about Sample type • Venipuncture blood • No blood stick

	Optimal		Minimal		
Number of Steps	Optimal: No more than 1-4 steps (requiring operator intervention)	**92%** **n = 12**	Minimal: No more than 4-6 steps (requiring operator intervention)	**64%** **n = 11**	6 comments as summarized below Theme: Variation in responses to 4-6 steps • Short, precise instruction required • Again, not sure on standards here but seems reasonable • 6 steps not feasible • Fewer is better, but 4-6 is okay for minimal • 4-6 steps is too much • How do we quantify this?
Calibration	Optimal: No calibration	**85%** **n = 13**	Minimal: Minimal user calibration required	**85%** **n = 13**	3 comments as summarized below Theme: Challenges with requiring calibration in certain settings • People won't calibrate • How do we quantify minimal? • If it does not need user calibration, that would be better especially in smaller hospitals where systems may not be robust • Optimal: Calibration will always be needed unless there is external QA
Kit Stability & Storage	Optimal: Stable for >12 months with harsh ambient conditions (temperature 5-45 °C, humidity 15% to 95%, dusty air, elevation >=2000 meters) and transport stress (48h with fluctuations up to 50°C and down to 0°C)	**100%** **n = 12**	Minimal: Stable for 12 months with harsh ambient conditions (temperature 10-40 °C, humidity 15%-95% elevation up to 2000 meters) and transport stress (48h with fluctuations up to 50°C and down to 0°C)	**92%** **n = 12**	3 comments as summarized below Theme: Is this technically feasible?
Equipment Required	Optimal: Small, portable or hand-held device; device-free/disposable preferred; does not require centrifuge	**85%** **n = 13**	Minimal: Small, table-top device; portable device optional; does not require centrifuge	**92%** **n = 12**	3 comments as summarized below • Concerns with theft of hand-held devices • The minimal and Optimal might be the same. Both should be small, but hand-held vs. table top does not give a clear advantage either way
Power Requirement	Optimal: None (i.e. a disposable test that requires no electricity)	**83%** **n = 12**	Minimal: 110-220V AC current; DC power with rechargeable battery lasting up to 8 hours of testing	**91%** **n = 11**	3 comments as summarized below • Does this mean it requires batteries? If so, I would rather have the rechargeable option • Does none mean batteries required? If so, I don't agree • "This category is not consistent with other similar battery backed up devices (pulse-ox, temp monitor). The product

	Optimal		Minimal		
					configuration requires some type of electricity. May need to separate and reformat category here."
Instrument Pricing	Optimal: <$200 ex-works	**91%** **n = 11**	Minimal: <$800 ex-works	**60%** **n = 10**	3 comments as summarized below Theme: $800 is considered high
Consumable Pricing	Optimal: <$0.50 per test ex-works	**100%** **n = 10**	Minimal: $1.50 per test ex-works	**78%** **n = 9**	3 comments as summarized below • No test (on the market or in development) will be able to meet the minimal currently. $2.00 is more feasible • Expensive. Around $1 may be okay

REFERENCES

[1] Clinical Laboratory Improvement Amendments of 1988 (CLIA) Proficiency Testing Regulations Related to Analytes and Acceptable Performance, 84 Fed. Reg. 1536 (proposed February 4, 2019). Retrieved from https://www.federalregister.gov/documents/2019/02/04/2018-28363/clinical-laboratory-improvement-amendments-of-1988-clia-proficiency-testing-regulations-related-to.

APPENDICES

Appendix A: Delphi-like Survey Respondent Organizational Designation

3rd Stone Design
Abuja University Teaching Hospital
Alex Ekwueme Federal University Teaching Hospital Abakaliki
Baylor College of Medicine
BC Children's Hospital
Burnet Institute
CCBRT Dar es Salaam
CENETEC-Salud
Center for Public Health and Development (CPHD)
Children's Hospital of Philadelphia
Christian Medical College, Vellore
Clinton Health Access Initiative
College of Medicine, University of Lagos
College of Medicine, University of Malawi
Dartmouth
Day One Health
Diamedica UK Ltd
D-Rev
Egerton University - Nakuru County Referral Hospital
ETH Zurich
Fishtail Consulting
FREO2 Foundation Australia
Global Strategies
Hawassa University
Independent Biomedical Engineer
Institute for Healthcare Improvement
intelms.com
Kamuzu Central Hospital
Kamuzu College of Nursing
Kemri-Wellcome Trust
Kenya Paediatric Association
Komfo Anokye Teaching Hospital
Malawi-Liverpool Wellcome Trust
Mama Lucy Hospital
Masimo
Mbarara University of Science and Technology
McGill University Health Centre
McMaster University
Medecins Sans Frontieres
Mediquip Global Limited
Ministry of Health, Senegal
mOm Incubators
MRC Gambia at LSHTM
Muhimbili National Hospital
Muhimbili University of Health and Allied Sciences (MUHAS)
Neopenda
No designation listed (10)
Pediatric and Child Health Association in Malawi

Pumwani Hospital
Queen Elizabeth Central Hospital
Rice 360 Institute for Global Health
Royal Children's Hospital and Centre for International Child Health (University of Melbourne)
Save The Children
Texas Children's Hospital
The University of Queensland
UCSF and London School of Hygiene & Tropical Medicine
UNICEF
University of Alabama at Birmingham
University of British Columbia
University of Global Health Equity
University of Maiduguri Teaching Hospital, Maiduguri
University of Nairobi
UNTH, Enugu

Appendix B: Consensus Meeting Participation

Albert Manasyan (University of Alabama Birmingham)
Anna Worm
Antke Zuechner (CCBRT)
Audrey Chepkemoi (Moi Teaching and Referral Hospital)
Bentry Tembo (Kamuzu Central Hospital)
Bev Bradley (UNICEF)
Casey Trubo (D-Rev)
Chishamiso Mudenyanga (Clinton Health Access Initiative)
Danica Kumara (3rd Stone Design)
Daniel Wald (D-Rev)
Edith Gicheha (Kenya Pediatric Research Consortium)
Emily Ciccone (University of North Carolina - Chapel Hill)
Emmie Mbale (PACHA)
Grace Irimu (University of Nairobi)
Guy Dumont (The University of British Columbia)
Helga Naburi (Muhimbili National Hospital)
Jeffrey Pernica (McMaster University)
John Appiah (Kumfo Anokye Teaching Hospital)
Jonathan Strysko (Children's Hospital of Philidelphia/Princess Marina Hospital)
Joy Lawn (London School of Hygiene and Tropical Medicine)
Lincetto Ornella (WHO)
Liz Molyneux (College of Medicine, Malawi)
Lizel Lloyd (Stellenbosch University)
Mamiki Chise
Marc Myszkowski
Maria Oden (Rice University)
Martha Franklin Mkony (Muhimbili National Hospital)
Martha Gartley (Clinton Health Access Initiative)
Mary Waiyego (Pumwani Maternity Hospital)
Matthew Khoory (mOm Incubators)
Melissa Medvedev (University of California, San Francisco; London School of Hygiene and Tropical Medicine)
Msandeni Chiume (Kamuzu Central Hospital)
Naomi Spotswood (Burnet Institute)
Norman Lufesi (Ministry of Health Malawi)
Pascal Lavoie (University of British Columbia)
Queen Dube (College of Medicine, Malawi)
Rachel Mbuthia (GE Healthcare)
Rebecca Richards-Kortum (Rice University)
Rhoda Chifisi (Kamuzu Central Hospital)
Rita Owino (GE Healthcare)
Robert Moshiro (Muhimbili National Hospital)
Ronald Mbwasi (Kilimanjaro Christian Medical Centre)
Sam Akech (KEMRI-Wellcome Trust Research Programme)
Sara Liaghati-Mobarhan (Rice University)
Sona Shah (Neopenda)
Steffen Reschwamm (MTTS)

Steve Adudans (CPHD/MQG)
Thabiso Mogotsi (University of Botswana)
Walter Karlen (ETH Zurich)
Zelalem Demeke (Clinton Health Access Initiative)

Appendix C: Abbreviations

°C	Degrees Celsius
bCPAP	Bubble continuous positive airway pressure
bpm	Beats per minute / Breaths per minute
CE Mark	Conformité Européenne – certification mark
cm	Centimeters
cm^2	Centimeter squared
CRP	C-reactive protein
CPAP	Continuous positive airway pressure
DHS	Demographic and health survey
FDA	Food and Drug Administration
HIS	Health information system
Hz	Hertz
IMR	Infant mortality rate
ISO	International Standards Organization
IV	Intravenous
KMC	Kangaroo Mother Care
kg	Kilogram
LPM	Liters per minute
LRS	Low-resource settings
MCH	Maternal and child health
MDG	Millennium Development Goal
Mg/dL	Milligrams per deciliter
mL/hr	Milliliters per hour
mmol/L	Millimoles per liter
µmol/L	Micromoles per liter
MMR	Maternal mortality rate
MNCH	Maternal, newborn, and child health
MNH	Maternal and neonatal health
nm	Nanometer
NMR	Neonatal mortality rate
PCT	Procalcitonin
PEEP	Positive end-expiratory pressure
PR	Pulse rate
RDS	Respiratory distress syndrome
ROP	Retinopathy of prematurity
SpO2	Peripheral saturation of oxygen
SDG	Sustainable Development Goal
TFR	Total fertility rate
U5MR	Under-5 mortality rate
UNFPA	United Nations Population Fund
USAID	U.S. Agency for International Development
uW	Micro Watts
W	Watt
WHO	World Health Organization