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NEST360°

Target Product Profile

Conductive Warmer – Thermal Management

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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

In general, newborns require a warmer environment than adults and the smaller the newborn, the higher the temperature needs to be. A newborn's ability to stay warm can be easily compromised by the temperature of its surroundings since newborn infants regulate body temperature much less efficiently than adults and lose heat more easily. Low birth weight and premature babies often face even greater risk [1].

As many as 85% of infants born in hospitals in low-resource settings become cold (defined as <36.5°C) [2]. Mortality rates increase with each degree Celsius of temperature lost. While the risks of being too cold are well recognized, hypothermia remains a largely invisible problem in overcrowded newborn units in low-resource settings. Hypothermia in newborns requires rapid diagnosis, which is often difficult in crowded and understaffed wards. Hypothermia not only increases the chances of acidosis, sepsis and RDS, but may indicate the presence of system illness such as infection or hypoglycemia.

Hypothermia can be treated using Kangaroo Mother Care (KMC), blankets/hats, warming cribs, warming mattresses, and Conductive Warmers. While hypothermia can be treated using KMC, infants and their caregivers may not be eligible for reasons such as, but not limited to: mother is recovering from surgery or the infant is in need of intensive care.

Attempts to warm a cold baby without monitoring temperatures carefully can result in hyperthermia. Rapid swings in temperature – known as thermal shock – can lead to negative outcomes, including death. Additionally, unrecognized fever in infants may lead to delays in treating neonatal sepsis and resulting in increased morbidity.

In high-resource settings, these negative outcomes are prevented by using incubators which continuously monitor and adjust temperature, or, with intermittent monitoring (every 3-4 hours) for infants who are in open cribs. However, incubators cost thousands of dollars and often require delicate sensors and expensive consumables. Existing temperature monitoring devices that are affordable in lower resource settings do not have the features necessary for the accurate detection of hypothermia or are not designed for a clinical setting.

In addition to the risks of hypothermia, pre-term infants and children are at high risk of infection, which can cause hyperthermia. A diagnosis of fever is not conclusive for any of these conditions, but it is a critical early sign of potentially severe illness. In combination with a respiratory rate monitor and pulse oximeter, continuous temperature monitoring can provide guidance to clinicians on what type of treatment to pursue; once treatment has begun, it can indicate whether treatment is working or needs to be increased.

Since low birth weight or sick newborns are most vulnerable to hypothermia, the World Health Organization has outlined various methods that can be used to keep high-risk babies warm including kangaroo-mother care, "warm rooms", heated mattresses, radiant warmers, and incubators. These methods vary in their response to addressing the four different ways in which newborns lose heat: radiation, convection, evaporation, and conduction [3].

Conductive warmers provide conductive heating either below or around the patient while also allowing health care workers with visibility and access to the baby. Given the high cost of some warming devices (e.g., incubator, radiant warmer), a need exists in low-resource settings for a technology that is both affordable and easy to use, and that can accurately detect hypothermia while keeping the newborn warm. The advantages of using warming devices include the fact that extra warmth can be given locally instead of having to warm the

whole room; temperature control is easier; and newborns can be fully observed and visible. The World Health Organization explains that different devices serve different purposes and advises that incubators are the proper choice for the care of very small newborns during the first few days or weeks. When these babies no longer have acute problems, they can be cared for safely on heated water-filled mattresses. Radiant heaters are best used for resuscitation and interventions where a number of people are involved [3].

Negative outcomes associated with hypothermia can be prevented using warming cribs that carefully control heat. Conductive warmers may be called warming cribs however are distinct from incubators. The intent in the development of this TPP was to provide developers with the opportunity to be innovative in the design process rather than be constrained by existing technologies or preconceived notions that a "crib" must be enclosed.

A need for the creation of a separate TPP for an incubator was identified at the Consensus Meeting. Incubators are the conventional method for maintaining normothermia in preterm and low birthweight neonates. Risks associated with incubator care include hypothermia [4,5]; hyperthermia [6]; nosocomial infections, related to lack of effective cleaning standards [7-9]; and cross-infection from other neonates when incubators are shared, a common practice in low-resource facilities. Failure of incubators to properly regulate temperature may be related to malfunction (e.g., over- or under-heating) [6,9-12], loss of electrical supply [13], ignorance of how to regulate set-points [6], as well as environmental factors [10]. In low- and middle-income countries, where there may be few nurses and doctors available, neonates in incubators may not receive adequate monitoring and serious events (e.g., apnea) may not be detected in time. Due to high purchase cost and poor routine maintenance practices, hospitals in such settings commonly face shortages of functional incubators [16,13-15].

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.

17 respondents participated in the Delphi-like survey for the Conductive Warmer.

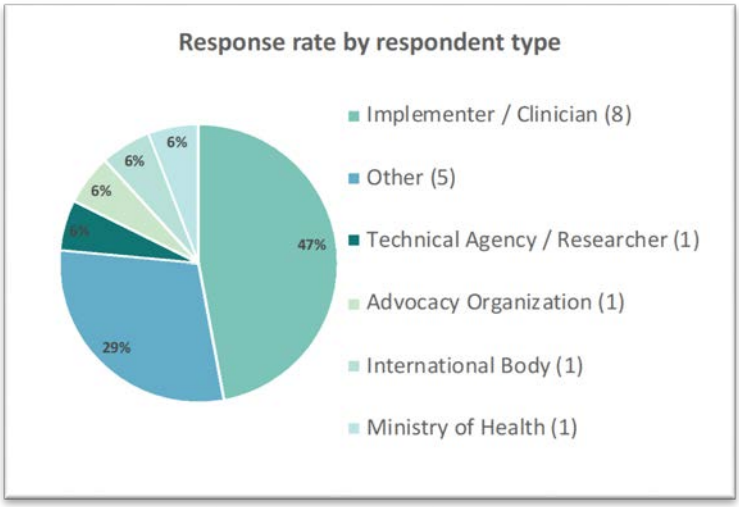
Survey respondents were requested to provide a statement on their level of agreement with each of the proposed characteristics for each TPP. Agreement was scored on a Likert scale ranging from 1 to 5 (1=disagree, 2=mostly disagree, 3= neither agree nor disagree, 4=mostly agree, 5=fully agree) with an 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.

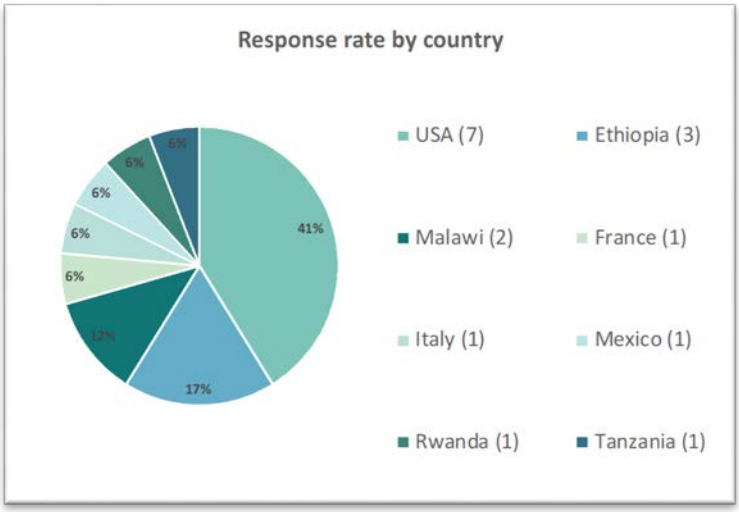
In total, over 180 organizations/individuals were asked to participate in this Delphi-like survey process, of whom 103 (see Appendix A) responded (response rate, 56%). Survey respondents were asked to self-disclose their affiliation.

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



Respondent type	Percentage
Implementer / Clinician (8)	47%
Other (5)	29%
Technical Agency / Researcher (1)	6%
Advocacy Organization (1)	6%
International Body (1)	6%
Ministry of Health (1)	6%

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



Country	Percentage
USA (7)	41%
Ethiopia (3)	18%
Malawi (2)	12%
France (1)	6%
Italy (1)	6%
Mexico (1)	6%
Rwanda (1)	6%
Tanzania (1)	6%

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 Conductive Warmer 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 - CONDUCTIVE WARMER

Final target product profile for Conductive Warmer		
Characteristic	**Optimal**	**Minimal**
SCOPE		
Intended Use	Treatment and prevention of hypothermia in neonates requiring thermal care	
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 [6]	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		
Form Factor	Enclosed or not enclosed (no preference)	
Benchtop Measurement Accuracy Conductive Surface Temperature **Temperature of Baby** (required if servo-controlled)	Conductive Surface Temperature: Accuracy of control of contact surface temperature (measured) = ± 1°C (and not exceeding 41°C) [1] Accuracy of baby's temperature: +0.2°C [2]	
Clinical Measurement Accuracy (Compare to another gold standard)	Known	Not required
Maximum CO2 Concentration (If Enclosed Device)	0.50%	
Maximum Temperature (of the conductive surface)	40°C [3]	
Humidification (If Enclosed device)	Humidity control for babies less than 1kg	None
Surface Temperature overshoot when the temperature control is set to its maximum setting	1°C [4]	
Time to Indicate Accurate Temperature of baby	< 90 seconds	<5 minutes [2]

Uniformity (If Enclosed, then uniformity of air) (If Not Enclosed, then uniformity of mattress)	Air Temperature: < 0.8°C (for enclosed only) [5] Conductive Surface (for enclosed and not enclosed) [2]: • High Heat: < 1°C • Low Heat: < 0.5°C	
Alarm Characteristics	Visual and Auditory	
Patient Interface	Interface is biocompatible and reusable	Interface is biocompatible
Patient Accessibility and Visibility	Patient is visible and accessible to healthcare worker	
Temperature Control	Based on infant's temperature and includes manual and failsafe mode	Manual control and includes fail-safe mode
Operating Conditions	Describe in user manual how warming device is impacted by ambient temperatures in the operating environment	
PURCHASING CONSIDERATIONS		
Consumables (probes)	> 12 months before required	> 6 months before required
Instrument Pricing	<$500 ex-works	<$1,000 ex-works
Consumable Pricing	<$50 per year ex-works	<$100 per year ex-works
UTILITY REQUIREMENTS		
Power Source	Mains Power	Mains Power
Power Consumption	<250W maximum	<800W maximum
Voltage	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)	
TRAINING AND MAINTENANCE		
User Manual	User manual and additional training materials (checklists, videos, guides) in at least one national official language for the country of intended use. Attached to device with labels and markings where possible	User manual provided in at least one national official language
Warranty	5 years	1 year
Decontamination	Easy to clean with common disinfecting agents	

[1] *Source: IEC 80601-2-35, Section 201.12.4.104* [17]

[2] *Source: ISO 80601-2-56, Section 201.101.3* [18]

[3] *Source: IEC 80601-2-35, Section 201.11.1.2.1.101.1* [19]

[4] *Source: IEC 80601-2-35, Section 201.12.4.103* [20]

[5] *Source: IEC 60601-2-19, Section 201.12.1.102* [21]

[6] *There was not 75% voting agreement on the Minimal characteristic. Please refer to the TPP Report discussion for additional detail.*

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Consensus Meeting Summary: Conductive Warmer

To arrive at the final TPP for Conductive Warmer (Table 31), a smaller group convened at the TPP Consensus meeting to determine which characteristics should be included in a brand new TPP for a Conductive Warmer. A need for a new TPP arose when it was determined that there separate TPPs were required based on the method of heating. Three methods of heating were outlined:

1) Radiant Heat (e.g., Radiant Warmer / resuscitaire)
2) Conductive Heat (e.g., Conductive Warmer)
3) Convective Heat (e.g., Incubator)

The smaller group discussion focused on the Conductive Warmer TPP as standards for incubators in high-resource settings currently exist. It was noted that there is a potential need for adjustment of these incubator standards for low-resource settings. Note that a pre-meeting survey for a Warming Crib was conducted and survey results are included in Table 32.

The following Product Specific Standards were highlighted:

- IEC 80601-2-35, Section 201.12.4.104 [17]
- ISO 80601-2-56, Section 201.101.3 [18]
- IEC 80601-2-35, Section 201.11.1.2.1.101.1 [19]
- IEC 80601-2-35, Section 201.12.4.103 [20]
- IEC 60601-2-19, Section 201.12.1.102 [21]

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, Conductive Warmer).

Delphi-like survey results for Conductive Warmer 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: Treatment and prevention of hypothermia in neonates requiring intensive thermal care.	**73%** **n = 11**	Minimal: Same as Optimal.	**88%** **n = 8**	4 comments as summarized below • Theme: Remove the word "intensive" • Theme: A variety of proposed Intended Use language o Optimal: treatment and prevention of hypothermia in stable and unstable at risk neonates not receiving (mother/caretaker not available) or not eligible (too sick or too small) to receive KMC o Optimal: Treatment and prevention of hypothermia in neonates requiring thermal care o Defining treatment as rapidly warming a patient and preventing hypothermia by safely keeping the baby normothermic - I would accept that a warming crib could only prevent hypothermia, as long as another device was available to rapidly warm a patient e.g. radiant warmer
Target Operator	Optimal: For use in low- and middle-income countries by a wide variety of clinicians, including	**100%** **n = 10**	Minimal: Same as Optimal	**100%** **n = 9**	0 comments

	Optimal		Minimal		
	nurses, clinical officers, and pediatricians.				
Target Population	Optimal: Neonates (<28 days)	**91%** **n = 11**	Minimal: Same as Optimal.	**100%** **n = 10**	2 comments as summarized below • Minimal: Neonates <28 days • Optimal: Minimal + treat babies over 28 days old e.g. KMC babies who have clinically deteriorated
Target Setting	Optimal: Hospitals in low-resource settings	**82%** **n = 11**	Minimal: Same as Optimal.	**100%** **n = 10**	4 comments as summarized below • Theme: Broaden Target Setting o Minimal: hospital in resource-limited settings, Optimal: health centres (primary) o Transport
International Standard	Optimal: ISO 13485:2016 Medical devices – Quality management systems -- Requirements for regulatory purposes.	**100%** **n = 5**	Minimal: Same as Optimal.	**100%** **n = 4**	0 comments
Regulation	Optimal: CE marking or US FDA Clearance	**86%** **n = 7**	Minimal: Same as Optimal.	**67%** **n = 6**	2 comments as summarized below • Theme: Reduce regulatory options or add more flexibility • CE Mark alone is sufficient
Benchtop Measurement Accuracy	Optimal: ±0.3°C	**80%** **n = 10**	Minimal: Same as Optimal.	**89%** **n = 9**	2 comments • Unclear what benchtop vs clinical accuracy means and how that would be measured/reported. Potentially combine? • +- 0.1 is Optimal
Clinical Measurement Accuracy	Optimal: ±0.5°C	**80%** **n = 10**	Minimal: Same as Optimal.	**89%** **n = 9**	2 comments • Assuming that this refers to the temperature of the baby e.g. through skin temperature probe, it is difficult to comment on what this number should be as we do not know deviance between bench testing (as above) and real-world. We can only really design to meet a bench-testing level • +-0.1

	Optimal		Minimal		
Heat Retention *(corrected from 'Pressure')*	Optimal: < 5°C loss over 4 hours	**78%** **n = 9**	Minimal: None.	**88%** **n = 8**	2 comments • In my mind, a warming crib should not lose heat but stay at a constant temperature • Is this the retention of heat within the baby or the device (mattress/air etc.)
Maximum CO2 Concentration	Optimal: 0.005%	**100%** **n = 7**	Minimal: Same as Optimal.	**100%** **n = 6**	1 comment • The CO2 concentration in air is approx. 0.04% so I think you may have an extra zero in the number • With incubators being a closed environment, the CO2 concentration will be higher at times. The International Standards leave manufacturers to specify a CO2 level following a specified test (IEC 60601-2-19 clause 201.12.4.2.101) • Atom, a recognized Japanese incubator manufacturer, state that the CO2 level for their V-2100 incubator is 0.4% following this test. Quote "CO2 concentration when stability has been achieved after administering air mixed with 4% CO2 to a point 10cm above the center of the mattress at 750mL/min doesn't exceed 0.4%."
Maximum Rate of Change in Infant's Temperature	Optimal: 0.5°C/hour	**75%** **n = 8**	Minimal: Same as Optimal.	**86%** **n = 7**	3 comments as summarized below • 1 degree per hour should be better • This is assuming closed-loop control with sensor. That was not mentioned above so may be confusing • In the case of incubators, there are specific standards to follow and we are not in a position to comment on how quickly a baby will warm up or lose heat as this will depend on their clinical state

	Optimal		Minimal		
Maximum Temperature	Optimal: 38.0°C	**56%** **n = 9**	Minimal: Same as Optimal.	**75%** **n = 8**	5 comments as summarized below • Should specify that this is referencing "Maximum Air Temperature" • Need to clarify what temperature this is. Is it baby, air, pad? • Maximum temperature should be 37.5°C • This may be specific to incubators (most of which actually go as high as 39°C) but feedback from all users indicate that they are never set above 36.5°C and rarely higher than 36°C (note, I refer to the temperature of the air, not the baby)
Overshoot	Optimal: < 2°C	**57%** **n = 7**	Minimal: Same as Optimal.	**50%** **n = 6**	3 comments as summarized below • Clarity on the parameter needed • Additional values were suggested o <0.5 o +-1 C
Time to Indicate Accurate Temperature	Optimal: < 90 seconds	**80%** **n = 10**	Minimal: < 3 minutes	**44%** **n = 9**	5 comments as summarized below • Clarity on the parameter needed • 3 minutes viewed as too long by respondents (e.g., 30 seconds suggested) but may not be technically feasible • Need to specify that it's clinical (not benchtop) and these are more realistic thresholds • Time to Indicate Accurate Clinical Temperature o Optimal: < 3 minutes o Minimal: < 5 minutes
Uniformity	Optimal: < 1°C	**100%** **n = 8**	Minimal: Same as Optimal.	**100%** **n = 7**	0 comments
Alarm Characteristics	Optimal: Visual and Auditory	**91%** **n = 11**	Minimal: Visual	**30%** **n = 10**	5 comments as summarized below • Theme: Minimal should include audio • Minimal could be turns itself off if certain temperature reached

	Optimal		Minimal		
					• What is alarm for? Baby temp?
Alarm Limits	Optimal: Adjustable	**64%** **n = 11**	Minimal: 36.5°C-37.5°C	**89%** **n = 9**	5 comments as summarized below • Clarify if air or baby temperature. Assuming this is air temperature rather than skin temperature, users would want the alarm to sound on deviation from set temperature • Adjustable may not be an advantage • Listing the alarm limits as adjustable is misleading, would propose updating to: o Optimal: +/-0.5 of baby set temperature o Minimal: 36.5°C-37.5°C
Consumables	Optimal: > 12 months before required	**100%** **n = 9**	Minimal: > 6 months before required	**100%** **n = 8**	3 comments as summarized below • Agree for almost everything, the exception being air filters which should be checked and possibly replaced after 3 months • Optimal would add some sort of automated features that lets you know when consumables needs to be replaced
Decontamination	Optimal: Easy to clean with common disinfecting agents	**100%** **n = 11**	Minimal: Same as Optimal.	**100%** **n = 10**	1 comment • Would it be helpful to use a "time to clean/disinfect"?
Maximum Power Consumption	Optimal: <250 Watts	**100%** **n = 8**	Minimal: <800 Watts	**67%** **n = 6**	2 comments as summarized below • 800 still high and not feasible at a solar system • Target minimal <500
Voltage	Optimal: 110-240V 50-60hz	**83%** **n = 6**	Minimal: 220-240V 50-60hz	**100%** **n = 5**	
Operating Temperature	Optimal: Harsh ambient condition, temperature 5-45 °C, humidity 15% to 95%, dusty air, elevation >=2000 meters	**78%** **n = 9**	Minimal: Harsh ambient temperature 10-40 °C, humidity 15%-95%, dusty	**75%** **n = 8**	3 comments as summarized below • Too strict and not realistic environmental conditions, would suggest changing to: Optimal: Harsh ambient condition,

	Optimal		Minimal		
			air, elevation up to 2000 meters		indoor temperature (20-40 °C), humidity 30% to 80%, dusty air, elevation <=2000 meters • An interesting question is raised when ambient temperature is greater than set temperature of the incubator
Patient Interface	Optimal: Interface is biocompatible and reusable	**100%** **n = 10**	Minimal: Interface is biocompatible	**78%** **n = 9**	2 comments as summarized below • Reusable should be part of the minimal requirement
Patient Accessibility and Visibility	Optimal: Patient is visible and accessible to healthcare worker.	**91%** **n = 11**	Minimal: Same as Optimal.	**90%** **n = 10**	2 comments as summarized below • Define visible and accessible
Patient Size	Optimal: Should fit a single infant <10kg	**73%** **n = 11**	Minimal: Same as Optimal.	**60%** **n = 10**	6 comments as summarized below • Theme: Should the warming crib fit more than one baby or not • This will be most critical in septic and new, preterm infants. So you need a lower limit (1kg) for which the warming crib also works • 10 kg seems large for a neonate • Should correspond to babies <28 days - 6kg max, 8 with contingency
Temperature Control	Optimal: Based on infant's temperature and includes fail-safe mode	**90%** **n = 10**	Minimal: Same as Optimal.	**78%** **n = 9**	2 comments as summarized below • For the incubator, temp control is based on air temperature. User research early on identified risks with patient temp control e.g. probes not properly attached. Agree fail-safe mode required - if temp runs higher than set temp • Should this also include a manual mode with simple settings? How does this spec limit developers to address the risks of multiple babies in one device?
User Manual	Optimal: User manual and additional training materials (checklists, videos, guides) in English and local language. Attached to	**100%** **n = 11**	Minimal: User manual provided.	**90%** **n = 10**	1 comment • User manuals are not used

	Optimal		Minimal		
	device with labels and markings where possible.				
Warranty	Optimal: 5 years	**91%** **n = 11**	Minimal: 1 year	**70%** **n = 10**	2 comments • Theme: 5 years too long | 1 year too short
Instrument Pricing	Optimal: <$500 ex-works	**78%** **n = 9**	Minimal: <$1,000 ex-works	**63%** **n = 8**	4 comments • These limits would not be relevant for Incubators, with volume, in the long-term, getting close to $1,000 could be achievable. • This is extremely expensive for a resource poor setting, considering the large number of patients which would benefit from this device
Consumable Pricing	Optimal: <$50 per year ex-works	**88%** **n = 8**	Minimal: <$100 per year ex-works	**86%** **n = 7**	2 comments • If referring to temperature probes these should ideally be cheaper as they will receive intensive use, thus requiring frequent replacement • The requirement for a battery may increase this. Excluding this $50 is aspirational and $100 is achievable but challenging.

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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