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Pneumonia Diagnostics Scientific Advisory Committee

Meeting report
Geneva, 17-18 June 2014

This document was prepared by Kevin Baker, Stefania Rigillo and Portia Reyes based on the Scientific Advisory Committee meeting held in Geneva, June 17-18, 2014.

Suggested citation:

Rigillo, S., Baker, K., Källander, K. (2014). Pneumonia Diagnostics Advisory Committee Meeting Report. London, Malaria Consortium.

The contributions of the Principal Investigator (Dr Karin Källander) and the international panel of experts, the assistance of Nicole Grillon (World Health Organization) and April Richardson (Bill & Melinda Gates Foundation) in the preparations for the meeting, the contributions of WHO staff from the departments of Child and Adolescent Health and Medical Devices and UNICEF Supply Division and the support of the Bill and Melinda Gates Foundation are gratefully acknowledged.

Cover photos: Malaria Consortium and Tine Frank (top left)

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Executive summary

An initial Scientific Advisory Committee (SAC) meeting for the project to evaluate respiratory rate and pulse oximetry devices for the diagnosis of pneumonia in children at community and first level health facility level was held in Geneva in June 2014. The meeting was attended by global representatives for UNICEF, World Health Organization, child health experts, diagnostics experts and country representatives from the four countries where the study is proposed to be conducted.

The objectives of the meeting were as follows:

- To brief the SAC and ratify the methodologies and stages involved in the project
- To ratify and agree on the Target Product Profiles for the respiratory rate and pulse oximeter devices to be used in the project
- To seek recommendations for advocacy and dissemination for the project results.

Overall, the SAC approved of the study and the protocols and activities presented. They highlighted the importance of the findings and its vital role in improving the detection of the symptoms of pneumonia in children under five in the community settings. The SAC also made several important recommendations for ways to improve the study design and ensure the results were as scientifically robust as possible. These included a request to ensure all of the stages of the study were documented and these protocols distributed and agreed with the SAC before implementation. The group also recommended the introduction of 'in-vitro' testing of devices before they are taken out into the field for evaluation. The group recommended the use of a reference standard rather than a gold standard, when comparing device performance. Regular updated were also suggested as a good check-in process as the project is implemented.

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Useful acronyms

ARIDA	Acute Respiratory Infection Diagnostic Aid
ARI (timer)	Acute respiratory infection
CHW	Community health worker
FLHFW	First level health facility worker
Pulse oximeter	Pulse oximeter
RR	Respiratory rate
SAC	Scientific Advisory Committee
TPP	Target Product Profile
UNICEF	United Nations Children's Fund
WHO	World Health Organization

Background

Pneumonia is one of the leading causes of death among children below the age of five years in both Asia and sub-Saharan Africa. Many pneumonia deaths result from late care seeking and inappropriate treatment due to misdiagnosis of symptoms. In response, several African and Asian countries are currently investing in community health workers (CHWs) to deliver life-saving treatment for young children, including antibiotics for signs of pneumonia. Diagnosis of pneumonia by CHWs and first level health facility workers (FLHFWs) is still largely presumptive and based on counting respiratory rate (RR) in children with cough or difficulty breathing to assess whether RR is higher than normal. However, counting RR is challenging and misclassification of observed rate is common, leading to wrong diagnosis and consequently inappropriate treatment[1-3].

Children who are taken for treatment late are at risk of developing severe pneumonia and the inability of health care workers to adequately recognise danger signs which indicate that the child needs urgent referral to a higher level of care, leads to the death of many children[4]. Hypoxemia has been identified as a predictor for morbidity and mortality in children with respiratory illness[5]. Pulse oximetry has been identified as a reliable and non-invasive tool to identify the levels of oxygen in children's blood as low levels of oxygen in the blood (hypoxemia) is a symptom of severe pneumonia; a strong predictor for pneumonia-related death[5]. But relevant devices are rarely available outside higher-level health facilities in resource-constrained countries[6].

For this reason, a growing number of research groups are focusing on innovative approaches to improving detection of pneumonia signs through the development of easy-to-use mobile phone applications and electronic devices. These tools focus on different approaches, such as measuring respiratory rate, heart rate, using automated accelerometers or cough/lung sound detectors[7-9]. The clinical performance, usability and acceptability of these tools in endemic settings are still largely unknown.

Day 1: Presentations and discussion

Introductory session

Presented by Dr Karin Källander, Malaria Consortium

Download at: www.malariaconsortium.org/news-centre/pneumonia-meeting.htm

Dr Källander from Malaria Consortium opened the meeting and presented on the background to the project as well as on the work Malaria Consortium has done in community case management over the years.

Dr Källander outlined the specific objectives of this first meeting of the Scientific Advisory Committee as follows:

- To provide an update on the Pneumonia Diagnostics project to the Scientific Advisory Committee (SAC)
- To discuss and agree on procedures and protocols for all of the research stages in this project
- To discuss updates from UNICEF on their ARIDA project and demonstrate the linkages between the Malaria Consortium project and the UNICEF procurement project
- To undergo an exercise to score device attributes following the MaxDiff methodology proposed by IPSOS Healthcare, a research agency from London
- To allow the SAC to have a closed session to elect Chair and Co-chair
- To discuss possible advocacy and communications activities to support the project.

Pneumonia Diagnostics project update

Presented by Kevin Baker, Malaria Consortium

This presentation focused on the research stages, providing an update on the current project status and facilitating discourse on possible issues that may arise.

Download at: www.malariaconsortium.org/news-centre/pneumonia-meeting.htm

The Malaria Consortium Pneumonia Diagnostics project aims to evaluate the use of various respiratory rate timing and classification devices, as well as pulse oximetry devices among CHWs and FLHFWs with different levels of training in Cambodia, Ethiopia, South Sudan and Uganda.

Malaria Consortium has selected these four countries due to the high proportion of under-five deaths caused by pneumonia in these countries. In addition, ministries of health in these countries are implementing programmes where pneumonia is diagnosed and treated at community level. Each CHW programme differs substantially across key areas, such as length of CHW training, CHW literacy levels and devices used to facilitate count of respiratory rates.

The project has systematically reviewed the landscape for existing tools and devices which could be appropriate for detecting the symptoms of pneumonia in low-resource settings. This process will identify the most promising and appropriate devices for field testing and establish their accuracy in supporting the diagnosis of pneumonia symptoms or measuring oxygen levels in the blood when used by CHWs and FLHFWs. Finally, the project will explore the devices acceptability and usability as perceived by CHWs, FLHFWs and caregivers.

The long-term success of this project will be measured by the large-scale uptake of easy to use, low cost and acceptable devices that will be available for global use in the community setting.

The current research stages were outlined as following:

- Stage 1 (Formative research): Focus group discussions on the current enablers and constraints experienced by CHWs in detecting the symptoms of pneumonia in children under five
- Stage 2 (Formative research): Pile sorting exercise to assess acceptability, feasibility and scalability with CHWs and national stakeholders in all four countries with up to 12 devices
- Stage 3 (Accuracy evaluation): Each tool/device (approximately six) measured several times against the reference standard measure with a varied sample of approximately 45 CHWs and 15 FLHFWs
- Stage 4: Pile sorting with 16 CHWs and six FLHFWs conducted to support the selection of two RR timers and one pulse oximeter (Pulse oximeter) device for routine practice evaluation
- Stage 5 (Routine field testing): Evaluation of user perceptions of devices in routine practice using 16 CHWs and 6 FLHFWs in each country over two months (240 and 90 interactions recorded with video)
- Stage 6 (Caregivers perceptions): One-to-one interviews with parents on their perceptions of devices (24 in each country)

The audience learned that the research will take 18 months from November 2013 and will include a device selection stage, a device evaluation stage and finally a dissemination of findings stage once the analysis has been completed.

Current enablers and constraints in detecting pneumonia at community level

Presented by Kevin Baker, Malaria Consortium

Following the update on the research stages, feedback was given in the focus group discussion recently accomplished as stage 1 of the project in all countries. The topics discussed in each of the three focus group discussions held in each country included: current enablers and constraints in diagnosing pneumonia at the community level, current devices used and the characteristics of an ideal device.

In general, the CHWs expressed they "felt" the need for diagnostic devices – i.e. when CHWs are not provided with a timer or other device to support counting respiratory rate, they will often substitute their own device, such as a mobile phone or a watch to support then in counting the second seconds required. The focus group discussions also highlighted the challenges the CHWs experienced in using the currently available devices such as the acute respiratory infection (ARI) timer and the counting beads.

Some of the issues highlighted from the experiences of the CHWs:

- Currently, CHWs have no experience of using pulse oximetry, including to detect of symptoms of severe pneumonia
- Issues with supply chain management for commodities such as ARI timing devices and medications hamper the effectiveness of the CHWs' efforts
- There is a need for more training as CHWs sometimes feel they suffer from a lack of skills
- The ideal device should be automated, have an improved level of usability and accuracy, be more durable, and more acceptable or believable to caregivers.

Fig 1: Participants at the SAC meeting

Discussion points: Day 1

The main discussion points following the presentations on the first day of the SAC meeting were:

- **The possible presence of fake devices:** Programme staff on the ground need to pay attention and consider whether fake devices are purchased and in use by CHWs, which can lead to poor performance and user disappointment with the device.

  Action: Malaria Consortium to investigate the presence of fake devices in all four countries.

- **There are different knowledge levels and exposure to devices in different locations:** In some countries and in very remote areas, even basic timers are not in use or are unavailable.

  Action: Malaria Consortium to document this in the landscape report.

- From a programmatic point of view, it will be challenging to select devices that have **consumables**, as it is extremely hard to replace batteries, sensors, etc.

  Action: Include this in the device scoring and ranking exercise as an attribute.

- For the devices to be included in the evaluation phase of our programme, it was discussed at which **level of development** they should be at to be considered; some devices could potentially appear relevant for the research and could match many of the requirements, but how long it could take for these to be ready to market must be thoroughly considered and assessed. **Delays in the development process may have implications on the overall project timeline and deliverables and must be closely monitored.** The final number of devices will be confirmed later this year (before the pile sorting exercise).

  Action: Allow for inclusion of products at different stages of development within the device selection process but limit it to devices which are market-ready or market-ready within six months.

- **Stage 4 pile sorting exercise**: It would be better to refer to this activity as 'stakeholder engagement'.

  Action: Revise plans based on SAC recommendations to refocus the pile sorting exercise to be a stakeholder engagement activity.

- Manufacturers were in general reacting positively to the request from the project team to have signed collaboration agreements in place. There were of course some doubts and queries in relation to ownership of intellectual property rights on the device – before, during or after the studies being done.

  Action: Malaria Consortium to ask their lawyers to redraft agreements to reflect the fact that ownership of intellectual property in relation to the device is not being held by Malaria Consortium or Bill & Melinda Gates Foundation.

- **Manufacturers should be included in the development process of the job aids**. The project team will facilitate dialogues between the job aid developer and the manufacturers.

  Action: A specific activity will be included in the planning of the job aid design and development.

- The project team need to **plan for the importation implications of the different devices** being evaluated. As some may not be FDA-approved, special requirements may apply – i.e. donated for research purposes and then taken back at the end of the study.

  Action: Malaria Consortium team to work with individual country teams to plan for this.

- **What happens if a device performs well in the pile sorting exercise in one country and badly in another one?** It was discussed whether it could be suitable to select different devices in each of the countries and its implications; an agreement was reached that the same devices should be tested in all locations.

  Action: The same devices will be tested in all countries.

- It was recommended to add an '**in-vitro' testing stage before sending the devices to the field**. This stage would involve laboratory testing to simulate field conditions, potentially delaying the shipment of devices to the countries and the start of stage 3. This activity would test both the potential devices' usability in the field as well as their accuracy in detecting the signs of pneumonia.

  Action: Malaria Consortium to source a suitable laboratory to conduct the 'in-vitro' testing.

- **During stage 3, ongoing checks on the functionality of the device should be ensured**, possibly through video recording CHWs using the devices and subsequently, have the recordings reviewed by a qualified expert. When a CHW detects hypoxemia with the help of a Pulse oximeter device, the required action is a referral to a hospital with oxygen facilities.

  Action: Malaria Consortium to change stage 3 protocol to reflect this in the study design.

- In case of referral, **availability of oxygen concentrators should be granted** in relevant health facilities and ensured by the programme.

  Action: Malaria Consortium to work with Bill & Melinda Gates Foundation to ensure this happens in all study sites.

- **Availability of CHWs and FLHFWs to participate in the research**: In designing the evaluation protocols, it should be ensured that the availability of health workers can be guaranteed and that sampling supports the ongoing requirements of the health system. Also, it will be necessary to define how many devices will be tested, if they can be tested at the same time, and how many measurements are required for a statistically valid evaluation. The risk of taking too many CHWs out of the health system at the same time must also be taken into consideration when defining the research protocols. The committee suggested increasing the number of measurements stated in the methodology from the original number per device of six.

  Action: Malaria Consortium to work with a statistician to review the sample size and protocols in the evaluation stage of the project.

Fig 2: SAC meeting participant from left to right: Dr Hailu Tesfaye, Dr David Peel, Dr Adriana Velazquez-Berumen, Kim Horn Hansen, Helene Möller, Stefania Rigillo, Kristoffer Gandrup-Marino, Kevin Baker, Dr Karin Källander, Prof Chhuoy Meng, Mark Newell, Dr Debbie Burgess, Dr Salim Sadruddin, Dr Shamim Qazi, Prof Rosanna Peeling

Day 2: Presentations and discussion

UNICEF: ARIDA project update and supply division overview

Presented by Helene Möller, UNICEF Supply Division

Download at: www.malariaconsortium.org/news-centre/pneumonia-meeting.htm

Helene Moller, Head of Health Centre at UNICEF Supply Division highlighted that the engagement of UNICEF with pneumonia and pneumonia diagnostics is very broad. The presentation aimed at providing an overview on how the organisation slowly shifted from direct delivery of supplies to providing procurement services, internally and to other organisations, until the creation of a specific supply division. UNICEF supply division procures over $2 billion per year.

Supporting pneumonia diagnostics at the community level led the unit to raise questions on the design specification of the devices, but it was not so easy to deal with manufacturers considering the issues of intellectual property and market monopolism. Although The ARIDA project had started already in the mid-80s with the distribution of timers, since 2005 there were renewed discussions between the World Health Organization (WHO) and Save the Children about the deficiencies of the tool, leading UNICEF to approach discussion for innovation of the ARI timer in 2007.

The main points relevant for consideration in the device innovation process were:

- Awareness of the user needs
- Introduction of new technologies in the procurement process of future pneumonia diagnostic aids

This process proved to be lengthy and was discontinued for several reasons, until the launch of a Target Product Profile (TPP) was finalised in January 2014.

Product innovation in UNICEF

Presented by Kristoffer Gandrup-Marino, UNICEF SD

Download at: www.malariaconsortium.org/news-centre/pneumonia-meeting.htm

The UNICEF Product Innovation team plays a role in developing the products themselves and/or enabling them to be developed. This means collaborating with partners in academia and in NGOs such as Malaria Consortium and setting up exclusive agreements with them to bring their product to the market.

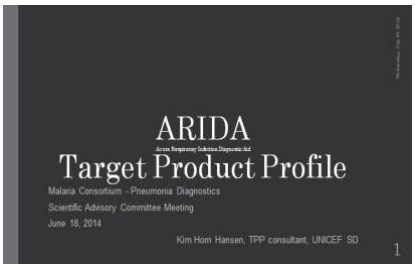
Regarding current involvement in pneumonia diagnostics, the UNICEF procurement project was assessed to potentially have a relevant impact on child health, and the further added value is that the TPP process is showing to be extremely suitable for replication across other innovation projects.

When discussing how to create an impact in the programmes implemented by UNICEF, the Product Innovation team concentrates on “nursing the promising plants”, but it also needs to provide an enabling environment for product innovation, ensuring the right “landscaping” to improve the growing conditions for relevant ideas.

It is also important to maintain continuous interaction in the field, to make sure the needs of final users are understood by industry and that clear lines of communication are maintained between all stakeholders – end users, suppliers and manufacturers.

UNICEF: ARIDA Target Product Profile (TPP)

Presented by Kim Horn Hansen, Consultant



Download at: www.malariaconsortium.org/news-centre/pneumonia-meeting.htm

The presentation introduced the scope of the TPP project. While UNICEF, WHO and other stakeholders have extensive knowledge of the users of diagnostic devices and their needs, industry and academia often have more knowledge on the technological aspects relating to the devices and how to manufacture devices. Therefore, it is hoped that in developing and implementing this tool, better knowledge transfer between the two sectors will be facilitated. Specifically, it is planned to:

- Communicate the context, needs and constraints for a diagnostic aid to be used for the diagnosis of pneumonia by a CHW in a resource limited setting
- Limit the scope to work within current integrated community case management (iCCM) and integrated management of childhood illness (IMCI) guidelines (i.e. fast breathing as a sign of pneumonia)
- The TPP is not a design specification
- The information is described at four levels of abstraction:
    1. Context description
    2. User and stakeholder needs
    3. Priorities
    4. Constraints
- Devices shall be analysed based on 18 parameters

At the moment, the draft TPP will be shared with partners and industry/academia for review, aiming to launch the final version by 19 August.

Max Diff product attribute exercise

Presented by Melissa Moodley, IPSOS Healthcare

Download at: www.malariaconsortium.org/news-centre/pneumonia-meeting.htm

The Advisory Committee and all meeting attendees were invited to participate in a scoring exercise based on 20 product attributes taken from the work done previously in the UNICEF TPP document.

This exercise will specifically identify which product features or attributes are most important in a diagnostic tool for the detection of signs of pneumonia for community health workers in low-income countries and rank them accordingly.

The methodology applied is the Anchored Max Diff:

- Instead of rating each attribute individually, respondents see several at one time based on a 'Latin-square' (balanced order and pairing) design
- Additionally, each attribute is presented and responses sought three times from each respondent which provides a more robust evaluation than a one-time assessment
- Respondents were also requested to rate each of the attributes on relative importance to the other attributes

The 20 attributes included are considered suitable for both RR and Pulse oximeter devices (see Appendix 3).

Fig 3: Measuring the blood oxygen saturation of one of the SAC members using the Lifebox Handheld pulse oximeter

Possible devices to be included in the evaluation

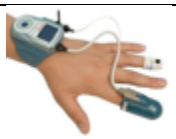
Presented by Kevin Baker, Malaria Consortium

As a result of the landscape analysis (10) already performed and taking into account the learnings of these two days, Malaria Consortium presented a list of possible devices for consideration by the SAC. The list is currently not yet complete and will be further worked on as part of the final device selection process in the next month or so, which will involve the SAC closely.

Table 1: Summary of possible devices for evaluation:

Method		Description	Device example & developer	Photo
Non-Automated				
Manual count (timer only)	**Analog device**	Timer used to inform the observer when to start and stop counting RR.	MK2 ARI Timer (UNICEF, WHO)	
Assisted count (aids visual counting)	**Counting beads**	Colour-coded string of beads eliminates the need for an observer to remember breath count and indicates diagnosis according to the child's age. Must be used in combination with a timer.	ARI Counting Beads (IRC, Save the Children)	
	Digital device	Standalone digital tally counter with built-in one-minute timer eliminates the need for an observer to remember breath count by having the user press a button to register each breath.	Philips Breath Counter	
	Mobile software application	Software-based mobile phone or tablet application with timer eliminates the need for an observer to remember breath count by having the user press a button or touch the screen to register each breath.	Rrate University of British Columbia Children's Hospital)	
Automated				
	Humidity	RR derived from oronasal moisture sensors measuring increases in humidity in exhaled breath.	respiR8®(Anaxsys Ltd)	

Exhaled breath	**Temperature**	RR derived from oronasal temperature sensors measuring increases in temperature in exhaled breath.	Respirometer (Profile Group of Companies)	*No photo available.*
	Air pressure	RR derived from oronasal sensors measuring increases in air pressure in exhaled breath.	Pneumotach (Hans Rudolph, Inc)	
	Carbon dioxide (ETCO2)	RR derived from oronasal capnography measuring carbon dioxide concentration in exhaled breath.	Capnomask (Mediplus)	
	Oxygen (ETO2)	RR derived from oronasal oxygen sensors measuring decreases in oxygen concentration in exhaled breath.	Datex-Ohmeda™ Ultima (GE Healthcare)	
Thoracic effort	**Thoracic circumference**	RR derived from belt sensors measuring changes in thoracic circumference with respiration.	Nox-T3 (Vivonoetics)	
	Thoracic motion	RR derived from sensors measuring changes in thoracic motion with respiration.	Beddit Sleep Tracker (Beddit)	
	Tidal volume	RR derived from electrodes measuring changes in lung volume with respiration.	Body Area Networks Health Patch (Holst Centre)	
Respiratory sounds	**Oronasal**	RR derived from acoustic respiratory signals collected from exhaled breath near the oronasal area.	Breath Counter 1.1 (Softrove)	
	Tracheal	RR derived from acoustic respiratory signals collected from the throat or neck.	Rainbow® Acoustic Monitoring Respiration Cloth Sensor (Masimo)	
	Thoracic	RR derived from acoustic respiratory signals collected from the chest, back, or armpit.	StrethoCloud (StrethoCloud)	
	Electrocardiogram (ECG)	Waveform morphology programs and signal processing techniques derive RR indirectly from	Actiwave Cardio (Vivonoetics)	

Indirect Effects on Cardiovascular Physiology		the ECG measured using ECG electrodes.		
	Photoplethysmogram (PPG)	Waveform morphology programs and signal processing techniques derive RR indirectly from the PPG measured using pulse oximetry.	Foxconn Smartwatch (Foxconn)	
	Arterial Blood Pressure (ABP)	Waveform morphology programs and signal processing techniques derive RR indirectly from arterial blood pressure.	Pulsewave™ Dx (BioSign)	
	Peripheral arterial tonometry (PAT) waveforms	Waveform morphology programs and signal processing techniques derive RR indirectly from PAT waveforms.	WatchPAT (Itamar Medical Ltd)	
Pulse oximeters	Mobile application	Oxygen values of the patient are shown on the display of the phone and can be easily understood by non-skilled CHWs. Free to download however does not include the cost of phone and external finger sensor	Masimo iSPO2	
	Fingertip Pulse Oximeter	Most affordable option for measuring oxygen saturation (SpO2) in blood. Almost all of these devices show values of pulse rate in addition to the SpO2	Contec	
	Handheld Pulse Oximeter	Suitable for adults, children and newborns, since oxygen is measured using a finger external sensor that can be purchased separately for paediatric and neonatal use. Tend to be more expensive than fingertip pulse oximeters and are designed for professional rather than for home use.	Lifebox	

	Wrist Oximeter	Shows several values (SpO2 and pulse rate only, or these plus other vital signs) on the screen. Transfers information via Bluetooth to a monitoring system, either on a computer or a mobile phone. No information available on their suitability for use with children and newborns.	WristClinic™	
	Any position pulse oximeter	Only one suitable device identified: Inspire™ which also measures respiratory rate and can be used with children and newborns in different positions.	Inspire™	

Discussion points: Day 2

Synergies between UNICEF and Malaria Consortium projects

- Medicines or devices supplied by UNICEF aim to be of high standard and quality, but this means sometimes price remains at a level that is not always affordable for some countries. UNICEF are aware of this issue and are currently tackling local capacity building for quality insurance and price negotiation, as it may be cheaper to buy locally, however, the risk to procure products that do not meet the other requirements could increase.
- For procurement of medical or diagnostic devices, it was discussed that defining the need is an essential first step, together with feasibility and technical specification.
- A search for consensus from participants of the meeting was made on the prioritisation of the devices' parameters.

  Action: Malaria Consortium and UNICEF projects' milestones to be aligned and a Memorandum of Understanding to be signed.

- It is important to define how the TPP process will impact and fit in the process followed by Malaria Consortium in its research study. In particular, an assessment is needed on how these findings overlap with those collected in the field by CHWs through focus group discussions.

  Action: UNICEF and Malaria Consortium should work together to align their projects.

- **To ensure that the device attributes are similar between UNICEF and Malaria Consortium,** it was confirmed that the two organisations aim to share and align the attributes as much as possible. This shall be facilitated with the involvement of IPSOS and their scoring exercise, which was designed by Malaria Consortium with IPSOS support in order to weigh the attributes more robustly. This will result in a sensitivity analysis of the same attributes present in the TPP.

  Action: A follow-up meeting to be held between UNICEF and Malaria Consortium to discuss the final lists of attributes.

- The result of the TPP should not be limited to one product. The ideal situation would be to have more than one device match with the TPP, one scoring high for price and others suited to match with the highest scoring attributes.
- It will be interesting to **compare the ranking** from UNICEF and Malaria Consortium surveys, to ensure consistency in both processes.
- Malaria Consortium designed the attributes bearing in mind the Pulse oximeter devices, while the UNICEF TPP focused on RR counters.
- A suggestion was raised that a small group will analyse the results from both studies, discussing **optimal and ideal parameters** as part of the TPP development process.
- To move from the TPP phase to a Request for Proposal, it was discussed that those aspects that cannot be compromise on should be included in the Request for Proposal.

Device evaluation parameters and protocol considerations

- Balancing the feedback from CHWs and other professional health workers as their scoring may be different.
- *Action:* Malaria Consortium to analyse this further.
- **It is important to define the absolutes** – what attributes the manufacturers should not miss, and the other attributes that are to be dealt with as priorities.
- **Reaching a consensus on priority parameters after both exercises from UNICEF and Malaria Consortium are completed to avoid confusion.**

  Action: Agreement to be reached at next SAC meeting.

- To make sure that all stakeholders agree on what will be needed from the devices, RR counters and Pulse oximeter devices will be added to an upcoming WHO 'Call for innovative health technologies for low-resource settings'.
- A query was raised on whether safety or high level of safety is an attribute to be ranked, and whether it should be ranked as an attribute or a constraint?

  Action: IPSOS will conduct an analysis with and without this attribute to see what the impact is on the final results.

- An agreement was reached to have a **reference standard instead of a gold standard**, as no suitable gold standard exists given the study is being conducted in resource poor settings. **This topic was discussed at the Technical Consultation held prior to the SAC meeting and the recommendations from this meeting were accepted (11).**
- **The selection of devices should be clearly stated and documented.**
- *Action:* Malaria Consortium to develop and circulate a detailed protocol for the steps in the device selection process. The SAC will be included in the final device selection.

Device selection practicalities

- **Market readiness is an important factor** that has an impact on the final device selection. If the market is not ready, this will delay the study.

  Action: Scoring to be conducted as part of device selection with the devices with more than six months development time removed.

- Technical specifications of the devices have been analysed on all devices where it was possible to get sufficient information. Devices' sensors information for Pulse oximeter was very poor with often no published data available.

  Action: 'In-vitro' laboratory testing to be performed to ensure that all devices taken into the field can perform accurately in the settings.

- **There is a need to check if all devices work with newborns.**

  Action: Malaria Consortium to include newborns in study design and definitions and suitable protocols to be developed.

- A quick decision is needed from Philips to know if they could meet the deadline for the inclusion of their device.

  Action: Malaria Consortium to contact Philips and check on device readiness to ensure its inclusion in the evaluation.

- **The suitability of various phone applications as diagnostics tools can further be assessed** once the ranking of devices is complete, as factors such as stability and usability are even more relevant for these devices.

SAC meeting participants gathering on day 2

Final recommendations from the Scientific Advisory Committee

Presented by Dr Shamim Qazi, World Health Organization

The SAC held a closed session to discuss and agree on their recommendations as a result of the discussions in the two-day SAC meeting. In the closed session, risks and opportunities associated with the programme were identified. A Chair and Co-chair of the Committee was also elected. The Committee Chair will be Dr Shamim Qazi and the Co-chair Prof James Tumwine.

In summary, the SAC recommendations are as follows:

1. Based on the concern that the device selection process was not clear enough and not documented with sufficient detail, the SAC requested that the project team prepare a table summarising the criteria adopted for the decision process and showing reasons for selection or exclusion of the devices throughout the selection process.
2. Devices to be tested should either be currently commercially available or within six months of being launched in the market, but only if they are considered as a possible device to detect the signs of pneumonia.
3. Devices should be tested in a laboratory ('in-vitro' testing) before being sent to the field to ensure they function under the required conditions prior field testing.
4. The Committee requested to be more involved in further steps of the research and in the selection process, with more face to face meetings specifically requested.
5. The SAC reminded the project team of the challenges of doing parallel evaluation in four countries with a large number of devices.
6. The SAC requested to receive fully documented research protocols defining in more detail the methodology for each stage of the study – device selection, device evaluation and field testing.
7. The SAC recommended that a reference standard be used rather than a gold standard and that the recommendations of the technical consultation (11) should be adopted for the study.
8. From an advocacy point of view, the SAC advised to make this project more visible and known through regular dissemination meetings at national, regional and international levels.
9. The SAC suggested further work should be done to ensure that no other devices are available which are not currently listed in the landscape review. Adriana Velazquez-Berumen of the WHO offered to request this information from a contact list of potential suppliers.
10. Devices which currently have high costs or run only as iPhone apps can be included at this stage. This is especially true if the technology can be transferred to an Android type system in the future.
11. Devices for newborns need to be more carefully researched and analysed, particularly before being field tested on newborns.
12. The SAC requested that the project team also consider developing mechanisms that can highlight potential diagnostic tools for future evaluations, i.e. ones that are still in development and not ready for testing now, such as the cough sound analysers.
13. The SAC requested that the project group seek to address the issue or risk that a device is tested and evaluated only for a newer version to be launched which supersedes it.

14. The SAC requested the project team to consider clinical trials insurance for the study.

Appendices and references

Appendix 1: Participants contact list

Scientific Advisory Committee:

Name	Affiliation	Contact	Present
Prof James Tumwine	Makerere University, Kampala	kabaleimc@gmail.com	Yes
Dr Hailu Tesfaye	Save The Children	hailu.tesfaye@savethechildren.org	Yes
Dominic Athian Dut	Ministry of Health, Aweil	dut.dominic@yahoo.com	No
Prof Chhuoy Meng	Calmette Hospital, Phnom Penh	mengchh@gmail.com	Yes
Dr Mark Young	UNICEF PD	myoung@unicef.org	No
Helene Moeller	UNICEF SD	hmoller@unicef.org	Yes
Kristoffer Gandrup-Marino	UNICEF SD	kgandrupmarino@unicef.org	Yes
Dr Shamim Qazi	WHO	qazis@who.int	Yes
Dr Adriana Velazquez-Berumen	WHO	velazquezberumena@who.int	Yes
Dr Debbie Burgess	BMGF	debbie.burgess@gatesfoundation.org	Yes
Prof Trevor Duke	RCH Melbourne	Trevor.Duke@rch.org.au	No
Dr David Peel	Ashdown Consultants	ashdownconsult@btconnect.com	Yes
Dr Salim Sadruddin	Save the Children	ssadruddin@savechilden.org	Yes
Prof Rosanna Peeling	LSHTM	rosanna.peeling@lshtm.ac.uk	Yes

Pneumonia Diagnostics team:

Name	Affiliation	Contact	Present
Dr Karin Källander	Malaria Consortium	k.kallander@malariaconsortium.org	Yes
Kevin Baker	Malaria Consortium	k.baker@malariaconsortium.org	Yes
Stefania Rigillo	Malaria Consortium	s.rigillo@malariaconsortium.org	Yes

Other participants:

Name	Affiliation	Contact	Present
Kim Horn Hansen	UNICEF - speaker	khhansen@unicef.org	Yes
Mark Newell	Global Good - observer	mnewell@intven.com	Yes
Melissa Moodley	IPSOS – speaker	Melissa.Moodley@ipsos.com	Yes

Appendix 2: Meeting agenda

Agenda Scientific Advisory Committee 17 June 2014			
Time	**Agenda item**	**Content**	**Presenter**
1:30 – 2:30	Introductions and project overview	Introductions, overview of workshop objectives and presentation of the project aims and objectives	Karin Källander
2.30 – 3.30	Project activity update 1	Detailed overview provides of different research stages in the project: • Device Selection (plus Q&A) DECISION POINT	Kevin Baker
3:00-3:30	**Coffee break**		
3:30 – 5:30	Project activity update 2	• Device Evaluation (plus Q&A) DECISION POINT • Device Field Testing (plus Q&A) DECISION POINT	Kevin Baker
5:30-6:00	Stage 1 Research findings	Presentation on the results of the focus group discussions on current constraints in diagnosing pneumonia by community health workers in resource constraint environments	Kevin Baker
6:00-6:15	Wrap up		Karin Källander

Agenda Scientific Advisory Committee 18 June 2014			
Time	**Agenda Item**	**Content**	**Presenter**
8:30-9.00	Recap of day 1	Recap of day 1 of the workshop	Karin Källander
9:00 – 9:45	UNICEF project update	Presentation on the background and stages involved in the UNICEF ARIDA procurement project	Kristoffer Gandrup-Marino / Helene Moller
9.45 – 10.45	Target Product Profile (TPP) – respiratory rate timers	Detailed presentation on the development of the TPP for respiratory rate timers and validation of the data DECISION POINT	Kim Horn Hansen
10:45-11:00	**Coffee break**		
11:00-12:00	Product attribute exercise	Presentation on the development of the Target Product Profile (TPP) for Pulse oximeter devices DECISION POINT	Melissa Moodley IPSOS
12:00-12:30	Possible devices for inclusion in evaluation stages	Presentation on the possible devices to be included in the evaluation and discussion with the advisory committee	Karin Källander
12:30-1:30	**Lunch break**		
1:30-2:30	Activity planning – next steps	Seek views from the SAC on potential advocacy and dissemination activities to support the project objectives and aims and discussion on next steps for device development and introduction at scale.	All
2:30-3:30	Advisory Committee closed session	Advisory committee side meeting to elect chair and co-chair, and discuss project activities, risks and opportunities	All SAC members only
3:30-4:00	**Coffee break**		
4.00-5:00	Feedback from advisory committee, wrap up, conclusions and close of meeting		All

Appendix 3: Device attributes

No.	Attribute	Description
1	Usability - ease of use	Easy for CHWs to use the device i.e. can apply it appropriately e.g. switch on the device, select the correct settings, complete the assessment to get a result
2	High level of decision support	Allows the community health worker to detect the symptoms of pneumonia without the need for decision making from them
3	Automation of diagnosis	Automatically provides the CHW with a diagnosis of pneumonia symptoms
4	High accuracy of measured/calculated result (e.g. RR/Pulse oximeter/etc.)	The device consistently provides an accurate measure of the result tested for – either RR or PO
5	No or little literacy and numeracy required	The device only requires a very low level of literacy and/or numeracy to be operated by the CHW
6	No or little training required	The CHW only requires minimal amounts of training to be able to use the device effectively to detect the symptoms of pneumonia
7	No or little familiarity with technology required	The CHW does not need any prior familiarity with technology to operate the device effectively to detect the symptoms of pneumonia
8	Long operational life in the field – e.g. more than two years	The device (not probes) will have an operational life while being used by CHWs of more than 2 years
9	Does not require charging (solar, battery, grid)	The device does not require charging to be used by CHWs to detect the symptoms of pneumonia
10	Does not require replaceable parts (non-rechargeable batteries, consumables)	The device does not require replaceable parts such as non-rechargeable batteries and/or consumables throughout its functional life in the field
11	Requires little or no maintenance	The device does not require any maintenance throughout its operational life when used by CHWs to effectively detect the symptoms of pneumonia
12	High durability/mechanical robustness	The device will not break during normal use by the CHW in the detection of the symptoms of pneumonia
13	High CHW confidence in measurements	The readings provided by the device support the CHW in relation to detecting the symptoms of pneumonia
14	High caregiver acceptability of diagnosis	The readings provided by the device help and support the caregiver/parent in accepting the diagnosis offered by the CHW
15	High patient comfort	The device does not cause hurt or discomfort to the patient while being used by the CHW in the detection of the symptoms of pneumonia

16	High portability	The device is easy to carry by the CHW during normal working
17	Easy to maintain hygiene	The device is hygienic and easy to maintain in this regard – i.e. doesn't require specialist cleaning procedures or products
18	Low price (less than $50)	The annualized device cost is less than $50 (Device = total package of device plus consumables such as batteries/probes and chargers)
19	High level of safety	The device provides a high level of safety when it is being used for the detection of the symptoms of pneumonia
20.	Multi-functional (includes a minimum of RR and Pulse oximeter)	The device incorporates several applications for the detection and classification of the symptoms of pneumonia

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