

**Global Pulse Oximetry Project**

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**Background Document**

**Table of Contents**

<b>1</b>	<b>INTRODUCTION</b>	
1.1	Project goals.....	1
1.2	Background .....	2-3
1.3	Pulse oximetry as a monitoring standard during anaesthesia.....	3-5
1.4	Why is universal pulse oximetry our goal?.....	5-8
<b>2</b>	<b>UNIVERSAL PULSE OXIMETRY ON A GLOBAL LEVEL</b>	
2.1	Challenges to achieving universal pulse oximetry.....	9-10
2.2	An estimation of the pulse oximetry gap.....	10-13
2.3	Other efforts to close the gap: the WFSA’s Global Oximetry project.....	14-16
2.4	Pulse oximetry training methods.....	16-19
<b>3</b>	<b>FROM DESIGN TO DISTRIBUTION</b>	
3.1	An effective low cost pulse oximeter for the developing world.....	20-23
3.2	Current product and manufacturing options .....	23-26
3.3	Introduction of new health technologies: lessons learned .....	26-31
<b>4</b>	<b>SUMMARY</b> .....	32

## 1. INTRODUCTION

### 1.1 Project goals

The goal of the Global Pulse Oximetry Project is to improve the safety of anaesthesia care throughout the world by providing affordable, robust pulse oximetry devices for every operating room in the developing world that does not have one. We will also develop a training program to improve provider response to hypoxemia. We will build upon the lessons learned from other efforts, such as the Global Oximetry project, which has improved pulse oximetry access and training in several resource-limited settings.

Evaluating the current barriers to universal pulse oximetry and understanding the differences in provider expertise in various hospital settings will be critical. In order to be successful, we must consider the following:

- Why is universal pulse oximetry our goal?
- Why does the “pulse oximetry gap” exist in the developing world?
- What is the true size of the pulse oximetry market?
- What is a viable design for an affordable pulse oximetry device?
- How would this device be effectively procured and distributed?
- How can we motivate clinical and political leaders to improve the safety of anaesthesia delivery?
- What type of training program will lead to effective and sustainable clinical improvement?

To identify a low cost pulse oximeter for the developing world, the World Health Organization (WHO) will define both required and desired specifications. This process may rely on existing technology, new technology, or a combination of both. We will consider the trade offs in the design of the power source, probe, features, and materials to ensure durability. At least one manufacturer will be chosen and a procurement and distribution plan will be developed. Conservative estimates suggest that at least 100,000 pulse oximeters will be needed to achieve our goal. Other market-based calculations suggest that as many as 1 million devices may be needed if additional settings such as post anaesthesia recovery rooms are considered. Working with manufacturers, procurement experts, and purchasers will be critical for this component of the project.

Finally, we will investigate different training programs that will ensure pulse oximetry adherence and sustainability. It will not be enough to simply purchase and distribute pulse oximeters without supporting the basic clinical skills needed to use them effectively. Implementing pulse oximetry in a universal fashion will require a concerted effort from WHO and its collaborators as it seeks to promote this standard globally.

## **1.2 Background**

For more than twenty years, the use of pulse oximetry for anaesthesia monitoring during surgery has been a standard of care in the developed world. Pulse oximeters are applied in nearly every procedure that involves anaesthesia or sedation. As a result of its universal application and other important advancements in anaesthesia safety and monitoring, anaesthesia death rates have decreased significantly over the past two decades. Most experts agree that the death rate solely related to anaesthesia in the developed world currently ranges from 1 in 50,000 to 1 in 200,000.<sup>1,2</sup> However, these safety practices have not been routinely implemented in the developing world. Estimates suggest that more than half of the operating rooms are not equipped with pulse oximeters. Anaesthesia death rates in these settings are reportedly 100 to 1,000 times higher than in the developed world.<sup>3,4,5,6</sup>

The reasons for this tremendous disparity are numerous. The severity of patients' conditions, inadequate clinical training, and poorly developed infrastructure are all important factors. The inability to appropriately monitor patients during surgery is another major contributor. Pulse oximetry, one of the most important monitoring tools, is often not available.

It is estimated that over 230 million surgical procedures are performed around the world each year.<sup>7</sup> This volume exceeds the number of childbirths globally, but with far higher death rates. As the developing world continues to modernize and life expectancy continues to improve, surgical volume is expected to increase significantly over the next several decades. In the developed world, 3-16% of hospitalized surgical patients have major complications and nearly 1% experience permanent disability or death as a result of their operation.<sup>8,9</sup> If these numbers are extrapolated globally, at least 7 million people will develop disabling complications this year, including 1 million who will die. Due to substantial differences in the safety of surgery between developed and developing countries, a disproportionate number of complications and deaths are likely to occur in resource-limited settings. Thus, the provision of safe surgical care has become a major global health priority.

To address these issues and improve the safety of surgery, WHO launched the Safe Surgery Saves Lives program in 2007. One goal was to define a minimum set of surgical safety standards that could be applied in all countries and hospital settings. The result was the creation of the WHO Surgical Safety Checklist, which was launched in June of 2008. Over 280 professional organizations, hospitals, and ministries of health have endorsed the checklist which includes a set of basic steps to follow before, during and after surgery.<sup>10,11</sup> These steps include confirming patient identity, documenting medication allergies, administering antibiotics on time, counting instruments, sponges, and needles, and ensuring that a pulse oximeter is on the patient and functioning. In total, 19 steps must be performed to complete the checklist. Only two require capital outlay: antibiotics – which are frequently given but on an inconsistent basis – and pulse oximetry.

At the time of the checklist launch, preliminary results from over 1,000 patients in eight pilot hospitals across the world were released by WHO. The checklist nearly doubled the chance that patients would receive proven standards of surgical care and substantially reduced complications and deaths.<sup>12</sup> As Dr. Margaret Chan, Director-General of WHO stated, “using the checklist is the best way to reduce surgical errors and improve patient safety.”<sup>12</sup> WHO is now leading the Global Pulse Oximetry Project which aims to make the pulse oximeter component of the checklist achievable in every operating room in the world.

### **1.3 Pulse oximetry as a monitoring standard during anaesthesia**

Initial efforts to establish pulse oximetry as a mandatory standard for patient monitoring during anaesthesia originated in the United States during the 1980s. Prior to that, standards for intraoperative patient monitoring did not exist. As a result, anaesthesia providers used intraoperative monitoring techniques in an inconsistent manner. These practice pattern variations likely led to an unnecessarily high number of preventable deaths related to anaesthesia. Though precise data describing anaesthesia mortality rates prior to the establishment of monitoring standards are sparse, at least three large studies were published in the 1960s and 1970s. More than 1.5 million patients were included in these studies which reported anaesthesia death rates ranging from 1 in 2,000 to 1 in 7,000 in the developed world.<sup>13,14,15</sup>

Citing concerns regarding this seemingly high death rate, Eichhorn and colleagues systematically reviewed all anaesthesia-related claims from nine teaching hospitals in the Harvard system from 1976 to 1984. Of the 15 intraoperative “accidents” or deaths, most were preventable with improved clinical vigilance and monitoring. From these efforts, the “Harvard standards” emerged, which represented the first set of formal guidelines for intraoperative monitoring.<sup>3</sup> The most important component was the continuous presence of an anaesthesia provider throughout the course of anaesthesia. Monitoring blood pressure, heart rate, ventilation and oxygenation were the other primary areas of focus. Pulse oximetry was one proposed method for providing continuous circulatory monitoring.

After publication of the “Harvard standards,” professional societies from around the world developed monitoring standards of their own. In 1986, the American Society of Anesthesiologists (ASA) adopted the “Standards for Basic Intra-Operative Monitoring,” which encouraged the use of pulse oximetry and capnography.<sup>16,17,18</sup> Three years later, the International Task Force on Anaesthesia Safety was formed to create an international set of anaesthesia standards. For the next two years, anaesthesia experts from around the world systematically analyzed the standards set forth by countries with established guidelines. Four levels of recommendations were outlined: “minimum” standards were applicable to any preplanned anaesthetic; further standards were to be implemented as resources and training permitted, starting with those that were “highly recommended,” and followed by those which were “recommended,” and then “encouraged.”

One of the principles espoused by the groups was the mandatory monitoring of tissue oxygenation; the use of pulse oximetry was “highly recommended” for this purpose.<sup>19</sup> In 1992, these “International Standards for a Safe Practice of Anaesthesia” were adopted by the World Federation of Societies of Anaesthesiologists (WFSA). When these standards were updated in 2008, the terminology was revised to provide only three levels of recommendation, which was consistent with those used by WHO. Standards that would be expected in all anaesthesia care for elective surgical procedures were termed “highly recommended,” which was the equivalent of a “mandatory standard.” Pulse oximetry was one of them. This was an upgraded recommendation to the equivalent of “minimum” standards in the original document. These new standards imply that pulse oximetry is now expected in all anaesthesia cases for elective surgical procedures.<sup>20</sup>

While it has been difficult to demonstrate a causal relationship given the multitude of changes in anaesthesia during the 1980s, the anaesthesia death rate fell significantly after widespread implementation of monitoring standards. A recent review of anaesthesia deaths in Australia from 1980 to 2002 confirmed that anaesthesia-related mortality fell significantly at the time of guideline adoption. The death rate is currently around 1 per 50,000 anaesthetics administered.<sup>2</sup> Another study from France documented a ten-fold decline in mortality since the 1980s. A death rate of 1 in 145,000 cases was cited by these authors.<sup>21</sup> In the US, Harvard investigators found a three-fold decrease in anaesthesia mortality after implementation of the standards. From 1985-1988, there was only 1 intraoperative accident and no deaths following administration of 244,000 anaesthetics.<sup>16</sup> Today, most anaesthesia experts would agree that the death rate attributable solely to anaesthesia in the developed world is between 1 in 50,000 and 1 in 200,000.<sup>1,2</sup>

Despite the adoption of these standards in the developed world and the subsequent decline in the anaesthesia death rate, there are still a disproportionate number of deaths from anaesthesia in the developing world. Death rates in some developing countries are 100 to 1000 times higher than in the developed world. In Zambia, 1 in 1900 patients die from anaesthesia-related complications.<sup>6</sup> In Togo, 1 in 150 surgical patients have anaesthetic complications which result in death.<sup>4</sup>

At the inception of the Safe Surgery Saves Lives project, the World Alliance for Patient Safety established a “Safe Anaesthesia” working group. Its technical paper states that “the most important monitor is the presence of the trained anaesthesia professional whose expertise is augmented by physiological information displayed by monitoring devices. Pulse oximetry is mandatory for every general or major regional anaesthetic.”<sup>22</sup> Pulse oximetry was subsequently established as a “highly recommended” standard for anaesthesia monitoring in WHO’s Guidelines for Safe Surgery.<sup>23</sup> As noted above, successful completion of the WHO Surgical Safety Checklist requires pulse oximetry during surgery.

#### 1.4 Why is universal pulse oximetry our goal?

It has been difficult to identify a specific reason for the decline in anaesthesia mortality over the past three decades. Improvements in monitoring, ventilator safety, and provider training all occurred during this time. Yet, most would agree that the implementation of monitoring standards was critical. These standards transformed pulse oximetry from a technology that was rarely used into an essential device in nearly every operating room in the developed world. They allowed anaesthesia providers to continuously monitor oxygenation and detect hypoxemia earlier. Anaesthesiologists no longer had to wait for clinical signs, such as cyanosis, to respond to a hypoxic patient. Consequently, technical mishaps such as circuit disconnection, airway dislodgement or obstruction, or inadequate oxygen administration were identified sooner and providers could respond before adverse events occurred.

Surprisingly, the relatively rapid inclusion of pulse oximetry into the anaesthesia armamentarium occurred without level one (randomized) evidence. In fact, most of the early data were observational. One of the most influential studies, published by Cooper and colleagues in 1984, involved 139 anaesthesia provider interviews. Over 500 “incidents” and 70 “critical incidents” were discussed with investigators. From these interviews, the authors determined that the leading cause of mortality was the failure to deliver adequate amounts of oxygen. Pulse oximetry would have made a difference in many of these incidents.<sup>24</sup>

Since Cooper’s study, there have been at least seven randomized controlled trials on pulse oximetry. One had inadequate postoperative data, which limited its usefulness for this discussion.<sup>25</sup> Of the remaining six, the study published by Moller and colleagues in 1993 was by far the largest and most informative.<sup>26</sup>

In this study, over 20,000 adults undergoing general or regional anaesthesia were randomized to either pulse oximetry or no pulse oximetry during surgery and in the postoperative recovery unit. The primary outcome measures were hypoxemia detection and perioperative and postoperative complications. The authors clearly state in the discussion that the study was not powered to detect differences in mortality. Nearly 2 million patients would have been needed to include mortality as an outcome.

Several critical pieces of information were obtained from this trial. Of utmost importance, the rate of hypoxemia detection increased nearly 20 fold in the pulse oximetry group ( $p < 0.0001$ ). Endobronchial intubation and hypoventilation were also detected more frequently. Patients with pulse oximeters experienced 50% fewer myocardial ischemic events than those without pulse oximeters ( $p = .03$ ). Cardiac arrest was also less frequent with pulse oximetry, although this difference was not statistically significant (4 arrests among 9,578 patients with pulse oximetry; 11 arrests among 9,772 patients without; 1 sided  $p$  value = .06).

Clearly, pulse oximetry benefited patients. It allowed identification of inappropriate airway management by revealing hypoxemia, and it decreased the

frequency of both myocardial ischemia (presumably by ensuring adequate oxygenation of the myocardium) and cardiac arrest. As expected, mortality rates were unchanged (3 deaths in oximetry group and 4 in the control) as were postoperative morbidity rates, which included respiratory, cardiovascular, neurologic and infectious complications.

Of the remaining 5 randomized trials which included nearly 1,500 patients, pulse oximetry consistently allowed early detection of hypoxemia by anaesthesia providers.<sup>27,28,29,30,31</sup> None showed a mortality benefit. Although a randomized trial of two million patients addressing the effect of pulse oximetry on mortality would be powerful, this study will likely never be done; pulse oximetry is the standard of care today, and most would consider further attempts at randomization to be unethical.

A recent Cochrane analysis of these trials concluded that the value of pulse oximetry “is questionable in relation to improved outcomes, effectiveness, and efficiency”<sup>32</sup>; most anaesthesia experts around the world would disagree.<sup>22</sup> Several retrospective reviews also strongly support the efficacy of pulse oximetry. One analysis of 2,000 anaesthesia-related adverse events showed a reduction in cardiac arrests when pulse oximetry was used.<sup>33</sup> Another review of 4,000 “incidents” in Australia and New Zealand revealed no cases of hypoxic brain injury from inappropriate ventilation after the introduction of pulse oximetry and capnography.<sup>34</sup> Oximetry alone would have detected 82% of the relevant incidents and 60% prior to organ damage. Capnography alone would have detected 55% and 43%, respectively.<sup>35</sup>

Capnography (carbon dioxide detection) is another modality that is recommended by most anaesthesia societies, including the ASA and WFSA. It allows detection of esophageal intubation and hypoventilation nearly 100% of the time and is the monitoring modality of choice for this purpose.<sup>36</sup> Yet, in resource limited settings, the benefits of capnography are less compelling than those of pulse oximetry. As Webb and colleagues have reported, pulse oximetry detects adverse events more frequently.<sup>35</sup> This is presumably because pulse oximetry detects hypoxemia, which is the most common cause of death as Cooper showed nearly 20 years ago. Furthermore, increased alveolar carbon dioxide concentrations from any cause (notably hypoventilation) can be detected early with pulse oximetry if the inspired oxygen concentration is maintained at or close to that in ambient air. By contrast, early hypoxia is not readily detected with capnography. Additionally, the cost and maintenance of oximetry are generally lower than capnography. For these reasons, pulse oximetry is the preferred monitoring modality in resource-limited settings.<sup>23</sup>

In summary, pulse oximetry has been the standard of care in the developed world for nearly two decades. Though randomized data suggesting a mortality benefit are lacking, both expert consensus and a large volume of published data indicate that pulse oximetry is beneficial for patients. Anaesthesia providers in all settings have demonstrated a strong commitment to pulse oximetry since its inclusion into anaesthesia care. There are exceedingly few drawbacks to pulse oximetry once providers are appropriately trained. In resource limited settings, universal pulse oximetry could substantially improve the safety of anaesthesia.



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## 2. UNIVERSAL PULSE OXIMETRY ON A GLOBAL LEVEL

### 2.1 Challenges to achieving universal pulse oximetry

Despite the establishment of pulse oximetry as a monitoring standard in the developed world nearly twenty years ago, it has been difficult to apply universally in resource-limited settings. In many developing countries, pulse oximetry is seen as a luxury, rather than a necessity. Inadequacies in financial resources, infrastructure and workforce are three critical factors that have impeded its widespread implementation.

The relatively high initial cost of pulse oximetry has been a significant barrier in many developing world settings. Most oximetry units cost at least several hundred dollars, with the exception of finger probe units which can be found for under US\$50. More sophisticated models incorporating multiple monitoring modalities can cost over one thousand dollars. Given the limited availability of resources, many government officials and public health leaders in the developing world have focused on other therapies which are perceived to be more cost effective. For example, for the cost of an average oximeter, two HIV patients could be treated with antiretroviral therapy for one year in India.<sup>1</sup> With respect to tuberculosis (TB), of the 22 countries with the highest burden of disease, the median cost of treatment per patient is nearly US\$300.<sup>2</sup> Maternal and child health issues have also received significant funding, as exemplified by the Millenium Development Goals which have committed billions of dollars to improve maternal and child health.<sup>3</sup>

Yet, if one examines the burden of disease attributable to surgical complications compared to tuberculosis, the numbers are fairly similar. In 2006, there were 9 million new cases of TB and nearly 2 million deaths globally. Funding for TB therapy exceeded \$3 billion in 2008.<sup>2</sup> During that same time period, 7 million people were disabled by surgical complications, and 1 million of these patients died as a result of their operation.<sup>4</sup> To address this challenge, WHO created the Surgical Safety Checklist, which requires pulse oximetry. This safety tool, combined with pulse oximetry, could substantially decrease the number of surgical complications and deaths. It is even feasible that the cost effectiveness of the Checklist and universal pulse oximetry could exceed that of TB treatment.

Poor infrastructure has also contributed to the limited availability of pulse oximetry in many hospitals in the developing world. This has adversely affected general surgical patients as well as pregnant mothers and their unborn children. One survey of more than 500 Ugandan hospitals that offer basic obstetric care revealed that most hospitals lacked a constant supply of electricity, running water, and functioning operating rooms.<sup>5</sup> Another survey of 97 anaesthesia providers in Uganda, who represented nearly one-third of the anaesthesia workforce, indicated that only 25% of providers had the necessary supplies to deliver safe anaesthesia to adults. Only 6% could deliver safe anaesthesia during a caesarean section. Electrical supplies were constant for only 20% of providers and 10% always worked without an oxygen supply. For three-fourths of

anaesthesia providers, the item most frequently unavailable was a pulse oximeter.<sup>6</sup> The situation is similar throughout sub-Saharan Africa and much of the developing world.

There are significant inequalities in the distribution of the world's 59 million health care workers.<sup>7</sup> For example, 10% of the global burden of disease exists in the WHO Region of the Americas. However, 37% of the world's health workers live there and 50% of the world's health finances are spent in that region. This contrasts sharply with the African Region where 24% of the global burden of disease exists. Only 3% of the world's health workers provide care in this region, and less than 1% of the world's health expenditures are spent there. This "workforce crisis" has profoundly impaired the ability of resource-limited countries to deliver surgical and anaesthesia care.

While a precise description of the anaesthesia workforce in the developing world is lacking, published data indicate a critical shortage. In Uganda, for instance, there are approximately 15 physician anaesthetists for a population of 27 million.<sup>6,8</sup> As a comparison, the U.K. has 12,000 physician anaesthetists for a population of 60 million – 600 times the number of anaesthesiologists per citizen. Due to the severe shortage of physician anaesthetists in Uganda, the vast majority of anaesthesia is administered by 350 anaesthetic officers in the country. These anaesthesia providers have, on average, only one to two years of anaesthesia training following high school.<sup>6</sup> The situation is similar in Cameroon, where more than 80% of surgical cases involve a non-physician anaesthetist.<sup>9</sup>

Given the scarcity of physician anaesthetists in the developing world, the vast majority of anaesthesia is administered by providers with limited training. While many of these "anaesthetic officers" are technically skilled, they often lack a thorough understanding of the relevant pathophysiology and have not received the training needed to anticipate or troubleshoot difficulties. Without adequate knowledge of the clinical implications of hypoxia, it is difficult to expect these officers to use pulse oximetry effectively for clinical decision making. This knowledge gap has limited the efficacy of pulse oximetry in these settings.

In other lower middle income countries, such as India, anaesthesia training has traditionally been limited to physicians. This has changed recently with WHO and WFSA statements supporting anaesthesia administration by medical officers with 1 or 2 years of training. Yet, the vast majority of anaesthesia is still provided by physician anaesthetists. As a result, while the quality of technical expertise is strong, the capacity to adequately treat the population is limited. Seventy percent of district hospitals have at least one physician anaesthetist, but only 22% of first referral hospitals employ physician anaesthetists.<sup>10</sup>

## **2.2 An estimation of the pulse oximetry gap**

No study has ever quantified the extent to which pulse oximetry devices are available to operating room personnel in low and middle-income countries. Even basic

information such as the number of operating rooms and the types of monitoring devices is lacking. Anecdotal evidence suggests the presence of an enormous and pervasive “pulse oximetry gap,” defined as the number of pulse oximeters needed to achieve 100% penetrance in a given setting. To estimate this “gap,” other data sources must be examined.

We must first estimate the total number of operating rooms in resource-constrained settings. This will give us a sense of the “operating room market.” Once this market is estimated, the gap in pulse oximeter availability can be evaluated. Given the universal use of pulse oximetry in high-income countries, the gap is assumed to be present predominantly in low and middle-income countries. Using 2007 Gross National Income per capita data, The World Bank has defined these types of countries as follows:<sup>11</sup>

- low income country: \$935 or less
- lower middle income country: \$936 - \$3,705
- upper middle income country: \$3,706 - \$11,455

Since an accurate estimate of the total number of operating rooms in poor and middle-income countries does not exist, and a time-consuming survey is impractical given our timeline, we identified two principle ways to estimate this:

- 1) Hospital bed-based calculation: WHO collects data on the number of hospital beds within a country, and the number of operating rooms can be derived from an assumed relationship between hospital beds and operating rooms within a hospital. Anecdotal evidence suggests that there are approximately two operating rooms for every 100 beds in the poorest of settings. This gives us a minimum estimated figure of approximately **208,200** operating rooms in low and middle-income countries.
- 2) Operative volume-based calculation: We have recently published an estimate of the number of major operations performed annually around the world.<sup>4</sup> The number of operating rooms can be derived from an assumed relationship between it and the number of operations performed in a country. If each operating room performs 3 cases a day and runs 5 days a week, or 260 days a year, there are approximately **124,780** operating rooms in low and middle-income countries.

In order to determine the immediate “operating room market” for pulse oximetry, we need to estimate the penetrance of these devices in operating rooms throughout a country, or conversely the “pulse oximetry gap.” Limited survey data suggest that pulse oximetry is present and functioning in 5% of the operating rooms in low income countries, 20% of the operating rooms in lower middle income countries, and 50% of the operating rooms in upper middle income countries. Using hospital bed and operative volume-based calculations of the total number of operating rooms, the immediate market for pulse oximetry is likely between **90,000** and **150,000** devices as shown in Table 1.

For comparison, we have also included in Table 1 an estimation of the potential pulse oximeter market based on population figures. If we wish to make a public health argument for pulse oximetry as an essential item for use in hospitals, we need to consider not only the hospitals that currently exist, but also those that should exist if a country were meeting the true needs of its population. By this estimate, if we assume that a country should provide one pulse oximeter for every 5000 people (a rough estimate of what is currently provided in developed settings), the total market for pulse oximetry in low and middle income countries is likely more than 1 million devices.

**Table 1. Pulse oximetry market estimates based on total number of operating rooms (from hospital bed and surgical volume extrapolations) and a population-based market assessment**

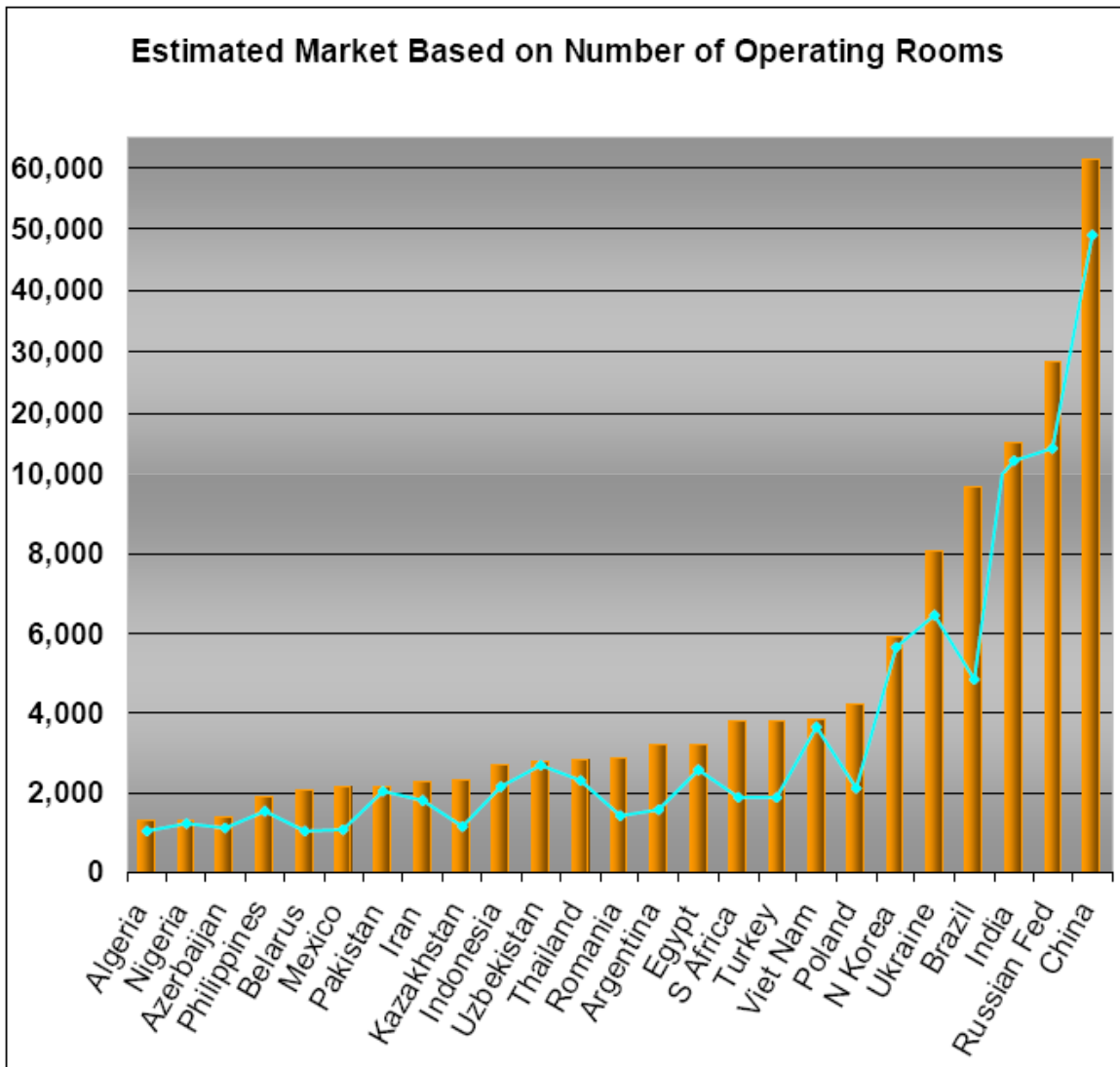
	Operating room market estimate based on number of hospital beds			Operating room market estimate based on operative volume			Population based market assessment
	# of operating rooms	Pulse oximeter penetrance	Pulse oximeter market	# of operating rooms	Pulse oximeter penetrance	Pulse oximeter market	Pulse oximeter market
Low Income	24,974	5%	23,725	8,385	5%	7,966	245,529
Lower Middle Income	112,151	20%	89,721	78,485	20%	62,788	679,813
Upper Middle Income	71,083	50%	35,542	37,914	50%	18,957	163,735
Totals	208,208		<b>148,988</b>	124,784		<b>89,711</b>	<b>1,089,077</b>

As demonstrated by the population-based estimate in table 1, which exceeds 1 million pulse oximetry devices, the hospital bed and operative volume approaches probably both underestimate the true pulse oximetry market. They do not take into account labor rooms, post anaesthesia recovery rooms, emergency rooms, intensive care units, and other areas where pulse oximetry clearly has a place in clinical evaluation and monitoring. They also do not account for the future market as surgical services increase in the developing world. There is a vast distance between what is currently provided and what is actually needed in terms of surgical services in much of the developing world. As countries address the shortfall of surgical services, the need for and use of pulse oximetry for safe anaesthesia monitoring will need to increase in parallel.

Figure 1 illustrates the pulse oximetry gap in the 25 countries where the gap is believed to be greater than 1,000 devices (note the change in units on the y-axis for those countries with a market less than 10,000 and those with a market greater than 10,000).



Figure 1. Immediate market estimate for pulse oximetry (blue line) and the total number of operating rooms based on number of hospital beds (orange bar). NB: there is a change in scale of the Y-axis at 10,000 devices.



To calculate the pulse oximeter market, we have used the operating room as the initial goal for distribution. Each operating room has been targeted for introduction of a standing pulse oximeter, thus making the item an essential monitoring technology. There is also the potential to target health personnel as a purchaser of individual, portable pulse oximeters. This would make the item an essential personal diagnostic tool similar to a stethoscope. Clinicians from specific specialties (such as anaesthesia, critical care, emergency wards, neonatal wards, and pulmonology) would find such an item of particular utility. However, for the purposes of this project, we have focused only on devices suitable for use in the operating room.

### **2.3 Other efforts to close the gap: the WFSA's Global Oximetry project**

During the 13th World Congress of Anaesthesiologists in Paris in 2004, the Safety and Quality of Practice Committee of the World Federation of Societies of Anaesthesiologists (WFSA) identified the provision of pulse oximetry during every anaesthetic in the world as a priority to improve patient safety. The WFSA, in conjunction with the Association of Anaesthetists of Great Britain and Ireland, and General Electric Healthcare (GE) created the Global Oximetry (GO) Project. Collaborating institutions included University of Manchester (UK), University of Auckland (NZ), the New Zealand Society of Anaesthetists, the New Zealand Vietnam Trust and the International Clinical Epidemiology Network (INCLLEN).

The aims of the Global Oximetry project were:

1. To set new worldwide standards for using oximetry in anaesthesia
2. To understand the barriers to sustained oximetry utilisation in such environments
3. To create appropriate oximetry solutions for low income and difficult anaesthesia environments

The first aim has been achieved. In Cape Town in March 2008, the revised International Standards for a Safe Practice of Anaesthesia mentioned above were endorsed by the General Assembly of the WFSA. In these standards the use of pulse oximetry is “highly recommended,” implying that it falls within the minimum standards for safe anaesthesia and is expected in all elective procedures. Similar wording is used in the recent WHO Guidelines for Safe Surgery, and a specific check to confirm that a pulse oximeter is on the patient and working has been included in the WHO Surgical Safety Checklist.

The second aim has yet to be achieved. WHO, through its World Alliance for Patient Safety, recognizes that this is an essential component of safe surgical and anaesthetic care and has committed substantial energy and time to move this issue forward. Oximetry, as previously discussed, is lacking in a substantial portion of the developing world. The availability of a low cost, highly robust, user friendly oximeter has yet to be introduced to a global market. While GE has remained supportive of the GO project, they have not yet committed to the development of a low cost oximeter.

Understanding the barriers to sustained oximetry use has been advanced through pilot projects which have introduced pulse oximetry in Uganda, Vietnam, India, and the Philippines. The oximetry gap was defined in specific areas where the project was to be undertaken, the use of donated oximeters was demonstrated through log books, and focus groups were used to understand the features of an ideal oximeter. In Uganda, ownership of the oximeters was placed in the hands of individual anaesthesia providers, while in the Binh Dinh province of Vietnam it was placed in institutions within the province. There was a more sophisticated anaesthesia environment in India, which provided its own challenges when introducing oximetry monitoring. In the Philippines, the project was undertaken in Cebu and involved the post-anaesthesia care unit (PACU).



GE Healthcare donated oximeters and provided training materials and logistical support in all four country projects. Pulse oximetry units with a plethysmographic display of the pulse (as a dynamic bar graph) and a pitch that varied with saturation level were considered suitable for continuous monitoring of anaesthetised patients and were deployed in the first three projects. A more basic, smaller, and inexpensive unit was deployed in Cebu and was considered suitable for use in the PACU.

There were a number of important findings that are relevant to any project hoping to improve the distribution and use of pulse oximetry worldwide. Several are discussed in other sections of this document: 1) there was a substantial gap in oximetry availability in both the operating room and in the recovery unit; 2) there was a clear but variable need for education of providers to interpret and respond to desaturation, both in the operating room and elsewhere in hospitals, notably the recovery units; and 3) there were a set of important features that will be integral to the development an ideal low cost pulse oximeter. A number of other lessons are also important to consider:

- Projects were most successful when permission from appropriate authorities was obtained in advance. Requesting assistance from local champions, including clinical personnel, administrators, and professional societies, was also powerful.
- Logbook data indicated that oximeters were used regularly when available. These data also showed that desaturation episodes were identified on a regular basis, and responses to these episodes were often appropriate.
- Many providers felt the need for oximetry in the PACU was equally important to that in the operating room. In addition, meeting the need for oximetry in the operating room led to greater use of oximetry in PACU as providers and administrators became convinced of its value.
- The oximeters used in the project were highly rated, as they were easy to use and robust. There were specific issues regarding some of their features, in particular the reliability of their power source and the sensitivity of their probes. While the probes were more vulnerable than the oximeters, they proved to be more durable than expected. At the end of one year, the majority of the original probes were still functioning and in use. However, different probes were needed for adults, children, and neonates.
- Pulse oximeter maintenance is of prime importance. For regular maintenance to be successful, it was essential to have a local supplier of parts and service who was easy to contact and responsive to the needs of the users. A budget allocated for the ongoing provision of maintenance and a clear protocol for identifying and repairing non-functioning units were also critical. In a number of places, oximeters were used in remote locations until problems developed (sometimes as simple as a flat battery), after which the oximeter was set aside until the next visit from a GO team member.
- The initial cost of an oximeter was less important in achieving universal use than convincing clinical and administrative personnel of its value in patient safety. However, the ongoing costs and logistics of maintenance, including the replacement of probes (which might prove more expensive over the life of

an oximeter than the initial cost of the oximeter itself), were not insignificant as noted in the previous point.

- Once introduced to the project, providers were willing to commit to the ongoing and appropriate use of oximetry. Interview and focus group data confirmed that participating providers were uniformly positive about pulse oximetry and strongly convinced of its value in contributing to patient safety.
- The key to promoting sustained change lies in working with local providers, hospitals administrators, and central government administrators to ensure that pulse oximetry is adopted as a standard of care and that its use is informed and appropriate. Local financial commitment must also be made to maintain the oximeters and replace probes and oximeters as needed. Clear systems for achieving this must be developed and maintained.

In summary, the gap in pulse oximetry is substantial in many parts of the world. A sustainable change in anaesthesia practice is achievable. Providing a suitable and affordable oximeter is one element in this. Maintenance is critical. Education is important. Engaging local providers and funders is also important, and in some areas it is likely to be essential.

#### **2.4 Pulse oximetry training methods**

In poorer parts of the world, most preventable anaesthesia morbidity and mortality is related to airway and respiratory problems leading to hypoxia. Hypoxia is difficult to detect clinically, particularly in dark skinned patients, and a pulse oximeter gives an early warning of these events. If anaesthesia providers can correctly interpret the information displayed by an oximeter and respond effectively to treat the cause of hypoxia and prevent it from worsening, many patients who might otherwise die during anaesthesia and surgery will be saved.

Although pulse oximetry is a relatively simple and reliable technology, successful use is dependent on a number of important issues. Providers need to know how to operate the oximeter, its alarms and menus, and how to attach it to the patient. They need to understand the common reasons for hypoxic readings in anaesthetised patients and how to diagnose the causes of hypoxia during anaesthesia. They also need to be able to interpret oxygen saturation in relation to the physiology of oxygen transport, taking into account the concentration of haemoglobin in the blood and any causes of increased metabolic rate (such as pregnancy, sepsis, etc.) and respond to hypoxia during anaesthesia. This includes the ability to distinguish artefactual readings. In addition to the clinical aspects of oximetry, providers and anaesthesia personnel must know how to maintain and clean the apparatus between patients and must understand how to maintain the charge in a rechargeable battery. The local arrangements for servicing or replacing a device and its probes are also critical for sustained oximetry use.

In order to ensure benefit from promoting the universal use of oximetry during anaesthesia, providers from a variety of backgrounds will need to learn how to use and

care for oximeters, how to interpret oximeter readings, and how to respond to hypoxia. This will require specific educational materials that are easily understood by all potential users. The Global Oximetry (GO) Project has piloted some educational material during its projects in Uganda, Vietnam, India and the Philippines. The experience of the project members is instructive and should be considered while developing the training program:

- Educational levels of anaesthesia providers varied significantly. The most sophisticated clinicians were well educated physician anaesthesiologists in financially constrained hospitals. There were also nurse anaesthetists and technically trained non-medical anaesthetists with appropriate knowledge and skill. Finally, there were providers with some practical skills but very little theoretical knowledge of medicine, physiology, pharmacology or anaesthesia.
- Highly trained physicians and nurses who are not familiar with the use of oximetry may not understand its fundamental concepts or what it hopes to achieve. Although it might be assumed that qualified medical personnel will understand the use of oximetry, this was not the experience in the UK following the introduction of this technology, nor of the GO project. However, such individuals have a reasonable base of theoretical knowledge to build on.
- The physiology of oxygenation and ventilation is quite sophisticated; simplistic and didactic teaching of oximetry is likely to lead to failures while interpreting the clinical situation. Alveolar ventilation, ventilation/perfusion ratio, shunt fraction, diffusion across the alveolar-capillary membrane, barometric pressure, inspired oxygen concentration, mixed venous oxygen concentration all influence the arterial partial pressure of oxygen. The delivery of oxygen also depends on cardiac output, the concentration of haemoglobin in the blood, and the oxygen-haemoglobin (Hb) dissociation curve which may shift in response to various physiological changes.
- Oxygen saturation readings must be correctly interpreted. Because of the shape of the oxygen-Hb dissociation curve, hypoxaemia starts to occur with oximeter readings below 90-93% and becomes rapidly worse. This is quite different to many examination systems, where marks of over 70% are regarded as very good. Even if a simplistic approach to teaching is adopted, this difference needs to be clearly understood.
- Language can be a significant barrier to educational initiatives. Materials can be translated, but it is difficult to be confident of the accuracy of the translation particularly in relation to more subtle concepts. The translation of medical terms and concepts is a specialised endeavour. Reading levels may also be variable and educational materials should strive to be as clear and succinct as possible.
- Many countries have at least some access to online web-based facilities. This creates the potential for interactive tools to teach physiological concepts. An example can be seen at the Virtual Anaesthesia Machine (VAM) website (<http://vam.anest.ufl.edu>) which includes a useful demonstration of the alveolar gas equation.
- Participants in these educational programs are typically adults experienced in the practicalities of providing anaesthesia in their own environment. Such

people tend to respond well to interactive educational techniques involving facilitated discussions (including discussions of case scenarios), questions and answers, and simulation (which can be fairly simple – see for example the VAM website). This approach, using translators if necessary, is more likely than didactic lecturing to identify failures in communication and conceptual understanding. It is also more flexible for responding to the actual needs of students.

- Evaluation is an important element of training and some form of testing is appropriate to ensure that educational objectives have been met. Documentation of educational achievement through certificates is usually appreciated.

As pulse oximetry is introduced into different countries and healthcare sectors, the learning requirements of anaesthesia providers should be assessed and training should be modified to account for this. The following recommendations should be considered as this training program takes shape:

- Resources should be as language-free as possible. This is facilitated by emphasizing graphical material rather than relying solely on texts.
- Notwithstanding the above, local language teaching materials are essential.
- Theoretical and practical training and assessment should be carried out for each anaesthesia provider.
- Specific anaesthesia scenarios and action plans for hypoxic patients should be included in the training materials and presented in an interactive discussion format.
- Local trainers should be recruited and trained, as this provides a sustainable mechanism for training colleagues in different parts of the country and in different hospitals.
- Reasonable time (ideally an entire day) should be allocated for both training during the initial introduction of pulse oximetry into a country or facility and for assessment of oximetry naïve anaesthesia providers.
- Supplementary training to reinforce educational goals and clinical skills should be provided at least annually during the first two or three years.
- Oximetry provides a focus around which many key principles of safe anaesthesia practice can be taught and illustrated.

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### 3. FROM DESIGN TO DISTRIBUTION

#### 3.1 An effective low cost pulse oximeter for the developing world

Any pulse oximeter should be judged by the degree to which a provider can monitor patients undergoing anaesthesia, interpret the data, and respond appropriately to the information provided in a given setting. Highly trained providers are more likely than poorly trained providers to have access to oximeters and adequate resources for their maintenance, even in low-resource settings. The cost of the machines, the logistics of their maintenance, their intuitive ease of use, and the education of anaesthesia providers are therefore highly relevant to clinical personnel providing anaesthesia without oximetry today. Thus, an oximeter which may be ideal in other respects is unlikely to be used on an ongoing basis unless:

1. Its life-time cost is affordable (including the costs of probes, maintenance and education).
2. The maintenance package and logistics are workable.
3. It is intuitive and easy to use.
4. Anaesthesia providers receive sufficient education to use the oximeter, interpret the information provided, and respond appropriately.

Experience from the GO Vietnam project illustrated a number of these points. Technician and physician providers successfully used a variety of donated oximeters from simple single-purpose units to complex and integrated ones. Yet, oximeters of all types and degrees of complexity were occasionally discarded because of perceived unreliability. Due to inadequate oximetry education, providers either misinterpreted correct indications of desaturation because they believed the device was unreliable or were not confident in adjusting the position of a probe to obtain a reliable signal. Failures in maintenance were also noted, with oximeters designated as “broken” simply because the battery was flat and the providers did not appreciate that several hours of charging is needed before any functionality would return. Oximeters were also consigned to the cupboard because the probe had broken and the providers had no mechanism for ordering a replacement due to lack of knowledge, protocol, or funding. The risk of this last point was highest for oximeters for which there was no local distribution agency, a common situation when using donated equipment. The ideal pulse oximeter may be defined more by the package with which it is provided than by its features.

A simple, portable and robust device providing only oxygen saturation and a pulse rate is likely to be more affordable, safer, and easier to use for providers with limited training. More complex monitoring which integrates other modalities such as capnography, non-invasive blood pressure, electrocardiogram and/or temperature is less feasible in these settings. Complexity may well imply the need for a more highly trained anaesthesia provider to interpret multiple signals simultaneously and relate this information to the clinical situation. Cost is less straightforward; saving money on an

inexpensive oximeter would serve little purpose if hospitals proceeded to purchase the other monitors as stand alone devices which resulted in higher overall costs. Thus if an integrated multi-modal device was affordable, robust, easy to use, and came with an excellent maintenance package and bundled educational material, it might be a good option.

Much of the surgery performed in low-resource settings is provided in circumstances of such severe financial constraints that capnography and automated blood pressure measurement are unlikely to be attainable. Therefore, the following comments will assume that the ideal low cost oximeter will be a stand alone device. Some allowance should be made, however, for imaginative solutions that go beyond the limits described below. Even if some integration of other modalities is offered, the following comments will still apply to the oximeter.

### ***Alarms***

Alarms are critical for any monitor. On a pulse oximeter they should alert providers to transgressions of safe limits of the oxygen saturation and to failures in obtaining a reliable signal. Alarms should be audible and supplemented with a visible change in the display (such as flashing). Alarms for one variable should be distinguishable from those of another and, if possible, should intuitively suggest the variable for which attention is required. The pulse tone should vary with the oxygen saturation (SpO<sub>2</sub>), with the pitch decreasing as the SpO<sub>2</sub> falls. It should be possible to vary the volume of the pulse signal and the alarm signals, but not to mute the sound altogether. A switch to override or mute alarms might be considered, but in such cases these alarms should be suppressed for less than 1 minute.

Default limits are highly desirable. It is debateable whether these limits should be configurable or whether it should ever be possible to disable the alarm altogether. An argument in favor of these two options relates to the possibility of using the device in patients with chronic causes of abnormal signals (such as cyanotic congenital heart disease). However, experience in the GO project has shown that defaults may be set to generally inappropriate limits for some specific reason and then left on indefinitely. The ideal default limits are probably the lower end of adequate oxygen saturation (90%) and the lower and upper limits of pulse rate (e.g. 50 and 120 beats per minute). Alternative defaults should be provided for paediatric patients. These defaults should be configurable on a case-by-case basis, but the device should return to its defaults each time it is restarted.

### ***Oxygen saturation***

Arterial oxygen saturation (SpO<sub>2</sub>) should be measured between clinically relevant limits (e.g. between 70-100%) with reasonable accuracy (e.g. within 2% of true saturation). This accuracy needs to be retained at low blood pressures (e.g. systolic of 50 mmHg) as well as high. The signal should be maintained in the face of some patient movement which may occur during general or regional anaesthesia.



### ***Pulse display***

The device should have a plethysmograph display of the pulse (either waveform or bar graph). The unit should measure pulse rate between clinically appropriate limits (e.g. 20 to 200 beats per minute) to an accuracy of  $\pm 3$  beats per minute. The pulse rate should also be displayed numerically.

### ***Ease of use***

The oximeter should be intuitive and simple to use. Its interfaces should be language free to the extent possible, although it may be appropriate to have configurable language displays. High and low alarm limits should be pre-programmed and, should they be adjustable, must automatically reset to default limits each time the device is switched on and off.

### ***Sensors/probes***

These are possibly the most critical part of an oximeter and over the life of the unit may be its most expensive component. They should be as robust as possible. A range of sensors covering various sizes and ages of patient should be available, including adults, children, and neonates. Both finger probes and ear probes should be available, and all probes should be reusable. Ideally an alarm should indicate sensor misplacement.

### ***Display***

The display should have optional backlighting which can be switched off during battery operation to prolong battery life. The readout should be interpretable from 5 meters.

### ***Connectivity***

Oximeters should ideally have internal memory to record readings and a printer port to print a patient's recorded parameters. It is also desirable to be able to connect this port to a computer.

### ***Power supply***

The device should operate at all commonly used power supplies (e.g. 240V, 50 Hz or 120V, 60Hz) or contain a converter for this purpose. It should have a rechargeable battery in case the power fails and for use when transferring patients. A fully charged battery should operate for at least 6 hours. A battery should take no more than 10 hours to charge, and charging should be possible while using the oximeter. A display of residual charge and low battery alarms are essential when operating on battery power.



The typical life of the battery should be known and should not be less than two years under normal use; the battery should also be replaceable.

### ***Physical features***

The dimensions and weight of the device should be specified by the manufacturer. Portability and ease of handling is desirable. The unit should be robust and should ideally withstand mishandling, including several drops onto a concrete floor from the height of the machine's normal working surface.

### ***Environmental issues and other specifications***

The machine should work reliably in a wide range of operating temperatures (e.g. 10°C to 40°C) and humidities (e.g. rH 15 to 95%). It should resist dust and mild exposure to liquids (e.g. water or blood). It should be easily cleaned with a disinfectant solution in case of bodily fluid contamination.

The oximeter should comply with relevant standards such as International Electrotechnical Commission (IEC) 60601-1 and International Standards Organization (ISO) 9919:2005. Where appropriate, it should carry a Conformity European (CE) mark.

### ***Warranties and maintenance***

The expected life of the oximeter and its probes should be specified and appropriate warranties provided. Provisions for maintenance should be described, including the contact details of the relevant suppliers, how much stock will be maintained of spare parts, whether the unit will come with spare parts to help with repair/replacement, whether support will be on a return to supplier basis, whether loan units will be provided during service, what turnaround times can be anticipated and what limitations will be placed on maintenance under warranty. An extended warranty or maintenance package would be highly desirable.

User and service manuals should be provided, electronically and by hard copy, in a variety of languages (which should be specified).

### ***Track record of company***

Information should be supplied on the year the model was introduced, the number that have been produced, and the size, global presence and track record of the company.

## **3.2 Current product and manufacturing options**

There are many different types of pulse oximetry monitoring devices available worldwide. They differ in cost, durability, accuracy, and the variety of information they are able to provide. The principle issue for the Global Pulse Oximetry Project is the

applicability of any individual unit for low-resource settings. As a general guide, pulse oximeters fall into three distinct groups:

1. Finger probe pulse oximeters intended for personal use.
2. Hand-held units or stand alone units which focus just on oxygen saturation and pulse.
3. Stand alone units which incorporate other parameters including ECG, capnography, or blood pressure monitoring.

When considering the benefits and drawbacks of these various units, the general specifications (discussed previously) must be considered.

### ***Finger probe pulse oximetry units intended for personal use***

While no single unit might have all features in a single probe, as a generalization, these units are able to measure SpO<sub>2</sub> and pulse as a waveform and a numeric digital display. They often have an adjustable alarm, are light, robust and can withstand adverse climatic conditions for use and storage. They frequently run on rechargeable batteries. Currently units of this type are available from US\$20 to US\$50. Some are priced as low as US\$10. While such a unit would appear to meet the basic requirements, it is difficult to determine performance. For example, how often will it give a false reading (either an unnecessary alarm or no alarm when the set parameters have been breached)? How often will the internal finger probes pick up the signal correctly and how often will they fail? Is the monitor easily tested for validity in its measurement? As most finger units do not have the option of using other probes, how long will the unit operate before failing? If it does fail are spare parts easily obtained so it can be repaired locally? Does it need to be returned to a distant location for servicing?

Part of the reliability comes from production standards. Have the units been produced to ISO standards and manufactured under Good Manufacturing Practices according to external assessment? Do the units meet electrical and other health product certifications?

Finally, the units must be easily adopted by clinicians in a range of health settings. Are the units easy to use? How much training might they require to use? Have the settings been designed to be easily adjustable?

### ***Hand-held pulse oximetry units***

In general, these units meet all of the monitoring specifications that the finger probe pulse oximeters include and have some additional features. The screen tends to be larger, brighter and easier to read. There are extra alarms, for example, for low battery power and poorly positioned probes. The addition of a cable running from the probe to the readout device means the screen can be positioned at a distance from the patient and a variety of probes can be attached depending on need (e.g. infants or adults). Both

disposable and reusable probes are available; however, the annual cost of disposable probes is likely to far exceed the cost of the instrument itself. Internal memory may be an added feature and can be useful to record patient data. Some have ports to allow printing of recorded data or downloading of information onto a computer. Currently prices range from US\$100 –US\$250 but may vary depending on the features of the machine. As with the finger probe units, performance, reliability, and ease of use must all be considered.

### ***Stand alone pulse oximetry units***

Such units meet all of the general specifications, as the finger pulse oximeters and small hand-held oximeters did, and have some additional features. The screen tends to be larger, brighter and easier to read than the other types of units. There are more alarms and indicators, both audio and visual. The software is more sophisticated, reducing false negative or positive signals; thus the accuracy tends to be improved. There are more power source options, with longer autonomous service. A wide variety of probes are available for use with these types of units. There is greater ability to store data for multiple patients over longer periods of time. Multiple modalities may be included, such as blood pressure and EKG monitoring. They are less portable than the other units and are less resistant to mishandling. Currently, prices range from US\$250- US\$1000; very sophisticated units may be priced well above this range however.

Ultimately the choice of units will be a compromise between utility, reliability and price. Surgeons and anaesthetists working in hospitals with strong financial support will likely want sophisticated units and will often be able to afford them. On the other hand, those working in low-resource settings will likely accept less expensive units if they meet their needs and bring them into compliance with monitoring standards.

### **3.3 Introduction of new health technologies: lessons learned**

Over the past twenty years there have been a number of comprehensive public health projects which illustrate important lessons regarding the optimal methods for introducing new healthcare technologies. The four-drug fixed-dose combination (4FDC) for tuberculosis (TB), auto-destruct syringes, weighing scales, pressure sterilizers, and oral rehydration salts are five examples which demonstrate how different products can be introduced into a global market. Each of these projects and the major lessons learned from their successes and failures are discussed below.

#### ***The four-drug fixed-dose combination (4FDC) for TB***

Treatment of tuberculosis involves the administration of a combination tablets (up to 12 at a time) for at least six months. Many patients find adherence to this regimen difficult and compliance is suboptimal. To improve patient compliance and reduce prescribing errors, four medications were combined into a single tablet.

Scientists and physicians were confident that the product would be beneficial, but manufacturers were reluctant to financially commit without a known demand. The Global Drug Facility (GDF) used donor funds to guarantee a market to a number of companies. One company proceeded to produce the 4FDC. The cost of production was borne by the manufacturer. Field observations of patient compliance were conducted by WHO. The initial cost per patient had been estimated at US\$15 but the final selling price was less US\$10. The market had been estimated at 25% of the TB market but quickly rose to more than 50%.

Independent laboratory testing for bioavailability of the product was initially difficult as there were no pharmacologic standards. After these were created and published, independent testing showed an error in calculation and the standards had to be rewritten. This caused delays in the project as errors in standards are unusual and were not anticipated. The development had been expected to take one year, but the product became available after 9 months, as an efficient process was created by involving a knowledgeable and enthusiastic producer.

While the initial purchase used donor funds, market countries rapidly took over the purchase of the 4FDC and now demand it in preference to other options. When the 4FDC was competing with other medications the selling price was under \$10 per patient. After the demand increased without competition, the selling price doubled to US\$20 per patient. The success in creating demand had given the sole producer a market advantage which resulted in the price increase; market dynamics had not been considered when creating this monopoly.

### ***Auto-destruct syringes***

The reuse of disposable syringes and needles was widespread in developing countries and low resource settings prior to the introduction of auto-destruct syringes. Reuse of disposable syringes resulted in increased numbers of nosocomial infections which threatened the acceptability of immunization programmes. Most believed that such infections could be avoided if syringes could only be used once, thereby prohibiting intentional reuse by health workers.

The market size was originally estimated at over 1 billion syringes per year for developing countries, with an additional, sizable, industrialized market to help provide higher profits to the producers. The developing country market assessment proved to be accurate. The industrialized country market however never materialized as reuse was not seen as a problem except for intravenous (IV) drug users. The IV drug users, as a group, refused to use auto-destruct syringes, even when they were made readily available.

The final selling cost had been estimated to be about 6 US cents or 50% higher than a regular syringe and needle. The actual selling price was 12 cents. Not coincidentally this was the price that had been set, confidentially, as the point above which the project would be abandoned.

It had been expected that as countries took over the purchase of their vaccines they would also buy auto-destruct syringes. However, countries continued to purchase regular disposable syringes despite significant scientific evidence of their risks and strong recommendations against doing so from WHO and other health agencies. Large volumes of auto-destruct syringes were purchased only after UNICEF decided that all injectable vaccines would be administered by them; UNICEF also agreed to pay for the syringes.

It had been expected that the product would become available within two years of program inception, but major distribution took four years. The original Expression of Interest attracted a large number of independent inventors - more than 500 submissions. Most designs were unworkable or not producible. The two designs that were eventually produced came from large syringe producers. The ability to fit within contemporary production lines was far more important than the brilliance of an innovative design.

The development costs were high and absorbed by either the inventors or the producers. One inventor spent more than 1 million dollars of his own funds without achieving success. The funds spent by the producers are unknown. Introduction into each country was expected to be difficult as the syringes did not allow nurses to aspirate for blood (a practice that accorded with their normal training). In fact, the nurses adapted to the new syringes very easily and introduction occurred mostly without training.

The original specifications preventing reuse were eventually slackened as creative methods of reuse were devised often by health care workers despite the best efforts of the manufacturers. The safety gains occurred from saturating the market with syringes, making reuse not only difficult but unnecessary.

### ***Health center weighing scales***

Numerous health projects needed to weigh neonates, children up to the age of five years old, and pregnant women as an important indication of health status. A wide variety of scales, many of them hanging scales, were designed and purchased for such purposes. Many of the scales could only do one job properly; a weighing scale designed to hold infants was not suitable for adults. The goal of this project was to replace all of these different scales with one scale that would work for all patients.

The estimated market size was 200,000 scales per year but the actual quantity was less than 30% of the estimate. Many country programs preferred to continue using familiar, though inferior, local scales rather than accept the new scales. A large, industrialized market was anticipated but never realized. The final product exceeded the original performance requirements in terms of accuracy and ease of use but could not be produced cheaply. The estimated cost was originally \$20 per unit but the actual final cost was \$80. Development and production of the scales were expected to take one year but took three years to become available.

The development involved a large investment by a donor/national government. Eventually, the investment was over 1 million dollars (ten times the original estimate)

and the project became impractical to abandon from a financial standpoint. After introduction, demand from other health projects and industrialized countries was minimal. The units worked well when they were supplied to country programmes but countries continued to choose other models when they had a choice. The original organization continued to financially support the technology.

### ***Pressure Sterilizer***

Reuse of syringes posed a significant threat to patients by increasing the risk of infections. The reuse of disposable syringes was difficult to prevent, particularly by health workers with inadequate supplies of syringes. Most believed that infections from syringe reuse could be avoided if a syringe sterilization process could be developed.

The market size for sterilizers was originally estimated to be about 250,000 units. No market was foreseen in industrialized countries, as industrialized countries preferred to use disposable syringes. The developing country demand estimate was found to be accurate. However, there was an unanticipated and profitable developed country market amongst dentists, veterinarians, and others who performed local sterilization.

The final selling cost had been estimated at about US\$50 and this was proven to be accurate. No estimates had been made for the selling price in industrialized markets, but it was much higher and became a profit center for the company. It had been expected that countries would take over the purchase of sterilizers but the market became saturated before this could occur. Nearly all purchases were financed by donors.

Product development was correctly projected to take one year. The original concept was presented to a major producer of pressure cookers and they liked the idea enough to fund all of the necessary research and testing. Because the project was managed by a major manufacturer, the time and cost estimates were detailed and accurate. Other producers were invited to compete after proof of product had been achieved. Eventually, another company entered the market but was unable to gather significant business as the efficiency of the delivery system quickly saturated the market.

The original specifications were closely adhered to and remain a WHO standard today. However, the efficacy of sterilization after introduction into market countries met with mixed results as many health workers never followed protocols suggested by the manufacturer. The original market analysis determined that the use of a sterilizer to disinfect reusable syringes 100 to 200 times was a cost saving system. In practice, the small numbers of patients and the high cost of fuel made this a more expensive option in many cases.

### ***Oral rehydration salts (ORS)***

Worldwide, diarrhea and subsequent dehydration is a major cause of death for children under the age of five. Dehydration can be prevented by drinking a very low cost



mixture of sugar and salt. Preparing such a mixture in a foil packet would enable parents of young children to have a suitable mixture available when needed.

The market size was expected to be large and this proved to be correct. The cost was correctly estimated to be less than 5 cents per mixture. The development time was expected to be about 6 months but was well over 1 year, as the difference in densities of the two major ingredients caused them to separate rapidly after mixing. This resulted in a non-uniform powder which caused many unexpected production problems for the pharmaceutical producers.

Countries were expected to purchase large volumes of ORS packets, but many chose other options. Home remedies to mix salt and sugar were adopted by some while others chose local production. These purchasing differences represented divergent policy views of numerous organizations; in many cases these differences were destructive to the project goals. Local producers of ORS lost significant revenue to overseas producers who could provide large shipments of ORS, often free of charge. Studies showed that home use mixtures were not as effective as imported foil packs because parents had difficulty replicating the ORS formulation. In addition, the development costs of the foil packs were borne by the producers, and many of them found these to be much higher than expected.

Introduction of ORS into each country required millions of health workers and parents to be trained in this new process, which was time consuming but generally successful. The original specifications were stringent because ORS was considered a pharmaceutical product even though it was composed of basic food items. There were few criticisms of the standards and they remained valid for decades.

***Major lessons learned from these five global health marketing projects:***

- International consensus should be obtained prior to proceeding with the project.
- Developing and introducing a new product is not an easy task and involves risk.
- Projects must be reevaluated every few months to analyze how the project and the environment have changed. Leaders must be willing to change directions according to project and market analysis.
- Forecasting may be inaccurate; trying to create new markets through public health officials is prone to error.
- There is a finite market for hard goods and once fulfilled, sales will decline.
- Any idea or prototype must be acceptable to the manufacturer and compatible with manufacturing processes. The manufacturer must accept and support the concept as it will bear most of the financial risk.
- The expected price and the final price may be very different and this will in turn affect the demand. Setting limits early in the process and continually examining costs as the project progresses will help calibrate expectations.
- Donors may be needed for the introduction stage and it may be difficult to move away from donor-funded products as the project progresses. The donor options must be carefully chosen.

- Sometimes small changes in specifications can result in very large changes in the cost. The negotiation between specifications and cost will be ongoing until production starts.
- Global delivery projects will usually take longer than expected.
- Once the product is in widespread use, deficiencies in specifications often become apparent. Agree if and how often specifications may change ahead of time.
- An awareness of the risks is important when creating a monopoly for a desirable product.
- Training programs are an important component of distribution and should accompany the introduction of a new product. Lessons learned from early adopters must be made available to others.



#### **4. SUMMARY**

Most operating rooms in resource-limited regions of the world do not have routine pulse oximetry monitoring. This “pulse oximetry gap” has contributed to the tremendous disparity in the safety of surgery between the developed and developing world. Conservative estimates suggest that more than 100,000 pulse oximeters would be needed to supply each of these operating rooms with a monitoring unit. To meet the needs in other clinical settings, such as emergency rooms, intensive care units, and post anesthesia recovery units, hundreds of thousands of additional oximeters would be required.

Financial limitations and provider inexperience are two critical factors that must be considered if we are going to close this gap. WHO’s Global Pulse Oximetry Project will address both of these issues by providing a robust, low cost pulse oximeter to the developing world and the training to use it effectively. By making pulse oximetry available in every operating room and improving clinician response to hypoxia, we will improve anesthesia care and surgical safety throughout the world.

To achieve this goal, experts from diverse backgrounds will be needed to solve the medical, public health, and business challenges that await us. Physicians, public health leaders, procurement and distribution experts, and manufacturers will be critical members of this team. Anaesthesiologists will be needed to discuss practical issues, such as design specifications and training methods. Procurement and distribution experts will help conceptualize and implement purchasing and distribution programs which may vary depending on the region of the world. Manufacturers will be critical for the development and production of a low cost pulse oximeter. With each group working together, this project has the potential to significantly reduce anaesthetic morbidity and mortality across the globe.