Pulse Oximeter Issues for May 13th Meeting

Anesthesiology and Respiratory Therapy Devices Panel

Introduction

The agency has traditionally accepted as evidence for clearance of a new pulse oximeter design, a comparison to a predicate pulse oximeter of similar design (i.e. reflectance, transmittance) and specifications (i.e. single use or re-usable, accuracy, motion tolerance), taking into account the area of application (e.g. finger, ear, forehead). The comparison usually looks at engineering bench testing for basic safety and clinical performance testing (i.e. desaturation studies) for an assessment of accuracy. The agency allows new/modified transmittance sensors to be compared to existing transmittance sensors and accepted accuracies < 3% as substantially equivalent for use on adults.

Sensor Type/Pt Population	Adult	Pediatric	Infant	Neonate
Transmittance wrap and clip	≤ 3.0 %	≤ 3.0 %	≤ 3.0 %	≤ 4.0 %
Ear clip	≤ 3.5 %	≤ 3.5 %	N/A	N/A
Reflectance	≤ 3.5 %	≤ 3.5 %	N/A	N/A

When this approach is applied to transmittance probes on neonates, we have traditionally allowed a 1% degradation of this accuracy since collecting controlled clinical studies on neonates to demonstrate accuracy is not ethical.

A new generation of reflectance sensors designed for neonates have tried to use their performance on adults as an indicator of their performance on neonates with this same allowed 1% accuracy degradation without any testing on neonates to confirm this accuracy. Another approach attempted to compare the performance of a reflectance sensor to a transmission sensor, usually at a different site. Performing controlled desaturation studies in the laboratory would produce ideal results; actual clinical results are likely to be worse. Hence there needs to be valid scientific evidence[1] of accuracy in neonates. Additionally, the agency is faced with the possibility of approving pulse oximeters for over-the-counter use.

Questions 1 and 2 seek guidance on what is the appropriate type of evidence to demonstrate clinical performance and what are the risks that need to be addressed in the neonatal application, both of transmittance and reflectance sensors. Question 3 seeks guidance on the risk/benefit tradeoff of allowing pulse oximeters to be marketed to the general public without prescription labeling.

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[1] Valid scientific evidence includes:
- Well-Controlled Investigations
- Partially Controlled Studies
- Studies & Objective Trials without Matched Controls
- Well-Documented Case Histories by Qualified Experts
- Reports of Significant Human Experience with a Marketed Device

Background on Reflectance V Transmittance

Pulse oximeter sensors may be implemented in either a transmittance or reflectance configuration. In both configurations, light is scattered by blood, which has time dependent characteristics, and bone or other tissue structures which are not time dependent. Transmittance sensors are configured in a manner where the emitter outputs light which travels through tissue (e.g. finger, toe, and ear) and is received on the opposite side by the detector. Reflectance sensors are configured with the emitter and detector in the same plane. Emitted light must reach the detector by reflection off a surface which typically results in smaller signal strengths in comparison to transmittance sensors. Significant differences in the tissue region sampled are a function of emitter/detector geometry. Differences in light propagation between the transmission and reflectance-based system would affect the relative amount of arterial blood sampled, average photon path length, the absorption characteristics of non-blood regions sampled (e.g. dermis, fat, bone, etc.).

The submissions we have been reviewing for reflectance pulse oximetry sensors are intended for use on the forehead or back of neonates. For clinical validation of new adult reflectance and transmittance oximetry sensors, we recommend a desaturation study on healthy adult subjects with 200 data samples taken from 70-100% SaO2. For transmittance sensors intended for neonates, we allow the manufacturer to add +/- 1% to the Arms accuracy specification clinically validated in the adult studies. This decision is based on the availability of literature on the effect of fetal hemoglobin on transmittance oximetry. There is evidence that fetal hemoglobin is not a clinically significant source of error. Similar literature is not available for reflectance oximetry over the whole specified accuracy range 70 – 100% SaO2.

Background on Over-the-Counter

The decision to allow a prescription device to be used over-the-counter (OTC) hinges on whether adequate instructions can be written for the layperson and whether the risks exceed the benefits. For pulse oximeters, there are existing non medical uses – mountain climbing and spelunking (high and low altitude) acclimation.

From REI's web site: an advertisement for a Nonin finger oximeter, a prescription device advertised for a non-medical use: (see following page)

Product Info

See specs below

This is **not** a medical device. It is intended to be used by climbers and other individuals enjoying activities at higher altitudes.

- Individuals who need a pulse oximeter due to a medical condition should contact their physician
- Or contact Nonin Medical at 800-356-8874, or Nonin's website at: mail@nonin.com for more information
- Mountaineering or trekking at high altitudes brings with it the potential for acute mountain sickness; SportStat™ may help alert you to its onset
- SportStat quickly provides accurate blood oxygen saturation and pulse rate data; feedback may help to assess the level of hypoxia at high altitude
- Easy to use instrument automatically turns on and off with finger insertion and removal
- Lightweight and compact in size, SportStat easily fits into a pocket or pack without sacrificing valuable space
- Bright display is highly visible in the dark; numeric display flashes once per second to indicate low batteries
- Durable and built to withstand the extreme conditions encountered in high altitude activity
- Moisture resistant; small amounts of moisture (as from rain) will not damage the unit
- Operates on two 1.5V AAA-size alkaline batteries for up to 1,000 spot checks of 45 seconds each (or approximately 12 hours of continuous use)
- Operates up to 30,000 feet (9,144 meters) and between +32 and +122 degrees F
- One year manufacturer's warranty

SportStat™ is ideal for spot-checking blood oxygen saturation and pulse rate. By simply inserting a finger into SportStat, you can obtain your blood oxygen saturation and pulse rate in a matter of seconds. SportStat takes the guesswork out of determining these important parameters, providing data that may alert you to the potential onset of acute mountain sickness (AMS).This is a valuable tool for anyone serious about high altitude mountaineering. Made in USA.

The instructions for use should be written so that laymen can understand and safely[2] and effectively[3] use the device. In order for a pulse oximeter to be marketed OTC, it must have adequate instructions for use per 21 CFR 801.5 (see following page). This means there needs to be adequate directions so that:

1. the oximeter can be placed properly,
2. any interferences (e.g. nail polish) or conditions (e.g. EMC) that would lead to inaccurate reading should be explained along with mitigating activities,
3. how to use the oximeter, including how long to wait, how frequently to measure, when to measure, what to do with the information, and how long to have the sensor on, are explained with an appropriate response, and
4. who should/should not use the oximeter is identified (e.g. age ranges).

Other factors to consider: mental and physical abilities of the user, ergonomic issues, the use environment, by whom will it be installed, the degree of control the user will have (setting changes), cleaning directions, maintenance.

[2] There is a reasonable assurance that a device is **safe** when it can be determined, based upon valid scientific evidence[3], that the probable benefits to health from the use of the device for its intended uses and conditions for use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks. The valid scientific evidence used to determine the safety of the device shall adequately demonstrate the absence of unreasonable risk associated with the use of the device for its intended uses and conditions for use.

[3] There is a reasonable assurance that a device is **effective** when it can be determined, based upon valid scientific evidence[3], that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results.

TITLE 21--FOOD AND DRUGS

CHAPTER I--FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCHAPTER H - MEDICAL DEVICES

PART 801 -- LABELING

Subpart A -- General Labeling Provisions

Sec. 801.5 Medical devices; adequate directions for use.

Adequate directions for use means directions under which the layman can use a device safely and for the purposes for which it is intended. Section 801.4 defines intended use. Directions for use may be inadequate because, among other reasons, of omission, in whole or in part, or incorrect specification of:

(a) Statements of all conditions, purposes, or uses for which such device is intended, including conditions, purposes, or uses for which it is prescribed, recommended, or suggested in its oral, written, printed, or graphic advertising, and conditions, purposes, or uses for which the device is commonly used; except that such statements shall not refer to conditions, uses, or purposes for which the device can be safely used only under the supervision of a practitioner licensed by law and for which it is advertised solely to such practitioner.

(b) Quantity of dose, including usual quantities for each of the uses for which it is intended and usual quantities for persons of different ages and different physical conditions.

(c) Frequency of administration or application.

(d) Duration of administration or application.

(e) Time of administration or application, in relation to time of meals, time of onset of symptoms, or other time factors.

(f) Route or method of administration or application.

(g) Preparation for use, i.e., adjustment of temperature, or other manipulation or process.