Pulse Oximeters and Addressing the Potential for Bias

As a result of the coronavirus disease 2019 (COVID-19) public health emergency, pulse oximeter usage has increased in both hospital and home settings. The US Food and Drug Administration (FDA) describes a pulse oximeter as a device that is typically placed on a fingertip and uses light beams to provide an estimate of the oxygen saturation of the blood (SpO_2) and the pulse rate. These non-invasive devices are widely used to obtain an indirect measure of arterial blood oxygen saturation (SaO_2), the gold standard for evaluating blood oxygen saturation levels.

Pulse oximetry is built on two physical principles: 1) arterial blood creates a pulsatile signal and 2) oxygenated haemoglobin (HbO_2) and reduced haemoglobin (HHb) have different absorption spectra.[1] Pulse oximeters typically emit light in the red and infrared wavelength regions (660 nm and 940 nm, respectively). More infrared light is absorbed by HbO_2, allowing red light to pass through, while HHb absorbs more red light and permits infrared light to pass through. The ratio of the red-light measurement to the infrared-light measurement is calculated for the systolic and diastolic phases. Afterward, the ratio of these ratios is calculated and converted to SpO_2.[2]

The FDA published the guidance for industry *Pulse Oximeters – Premarket Notification Submissions [510(k)s]* in March 2013 to assist sponsors in preparing 510(k) submissions for pulse oximeters.[3] It covers class II devices regulated under 21 Code of Regulations (CFR) 870.2700 for oximeters and 21 CFR 870.2710 for ear oximeters. Of note, these devices are categorised as prescription-use pulse oximeters that undergo clinical testing and FDA review before being granted 510(k) clearance. The guidance includes recommendations on topics such as how to evaluate the accuracy of pulse oximeters and what to include in labelling.

Limitations of Pulse Oximetry

In December 2020, results were published in the *New England Journal of Medicine* about the potential for racial bias in pulse oximetry measurement.[4] The findings described in the article suggested that pulse oximeter readings may not be as accurate in people with darker skin pigmentation. Relying on pulse oximetry to adjust supplemental oxygen levels may increase the risk of hypoxemia for this population, the authors noted.

This article was referenced in an FDA safety communication issued in February 2021.[5] The agency notified patients and healthcare providers that pulse oximeters "have limitations and a risk of inaccuracy under certain circumstances." They were advised to not rely solely on pulse oximeters to assess oxygen levels and to be aware that factors such as poor circulation, skin pigmentation, skin thickness, and skin temperature can affect pulse oximeter readings. Additionally, the FDA specified that over-the-counter (OTC) pulse oximeters, which saw increased use due to COVID-19, do not undergo FDA review and are not intended for medical use.

Re-examining Current Regulations

Among its efforts to address the limitations of pulse oximetry, the FDA sought feedback from the Anesthesiology and Respiratory Therapy Devices Panel (ARTDP) of the Medical Devices Advisory Committee (MDAC). A meeting was held on November 1, 2022, focusing on the concern that pulse oximeters may be less accurate in individuals with darker skin pigmentation and the potential factors that affect pulse oximeter accuracy and performance. The ARTDP members acknowledged the disparate performance of pulse oximeters in this patient population. They recommended that future studies on these devices assess a full spectrum of skin pigmentation, that the labelling for pulse oximeters include a statement on their possible inaccuracy in relation to skin pigmentation, and that OTC pulse oximeters should indicate that they are not intended for medical use or clinical decision-making.

After this meeting, the FDA published the *Approach for Improving the Performance Evaluation of Pulse Oximeter Devices Taking Into Consideration Skin Pigmentation, Race and Ethnicity* to share a potential clinical study design that can incorporate a larger range of skin pigmentation.[6] As noted in the discussion paper, the 2013 FDA guidance recommends that a study should involve participants with a range of skin pigmentation but does not explain how or at which site on the body to assess skin pigmentation. Elements of the proposed clinical trial include enrolling participants that span the entire Monk Skin Tone Scale (MST) and evaluating MST values at locations with a wide range of pigmentation levels (*e.g.*, the forehead).

On February 2, 2024, the ARTDP reconvened to provide feedback on the discussion paper and consider other data that should be provided by manufacturers to the FDA. The panel members supported the use of the MST and the approach of evaluating it as an initial assessment of skin pigmentation, followed by an objective pigmentation assessment such as individual typology angle (ITA). However, they also had some critiques of the proposed clinical study design. For example, several panellists noted that the minimum sample size suggested by the FDA (24 participants) may not be sufficient. Because premarket studies generally include healthy participants and are conducted in controlled settings, the ARTDP emphasised the need for real-world data (RWD) to ensure that the devices perform as intended for patients.

Ongoing Efforts to Assess the Performance of Pulse Oximeters

Regarding RWD, the FDA has funded grants to the University of California San Francisco (UCSF)–Stanford University Center of Excellence in Regulatory Science and Innovation (CERSI) for two real-world, prospective clinical trials that are assessing pulse oximeter errors related to skin pigmentation in hospitalised adult and paediatric patients.[7–8] Both studies are designed to measure several parameters, including SpO_2, SaO_2, and the site of pulse oximeter probe placement, across different patient groups. Additionally, skin pigmentation is being measured via colorimetry tools such as the MST, the Fitzpatrick Skin Type Scale, and the von Luschan's Chromatic Scale.

At the February 2024 ARTDP meeting, updates for each trial were provided by the study coordinators. Among their findings thus far, they have observed that the probe location varies in the real-world setting, and some pigment scales correlate moderately with ITA values. The FDA has yet to update its 2013 guidance

on pulse oximeters but noted that it intends to reassess current recommendations based on stakeholder feedback, results from the published literature, and outcomes from the UCSF-Stanford real-world studies.

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