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Center for Devices and Radiological Health
Food and Drug Administration
10903New Hampshire Avenue
Building 66, Room 5216
Silver Spring, MD 20993-0002

Submitted Electronically: http://www.regulations.gov

Re: Approach for Improving the Performance Evaluation of Pulse Oximeter Devices Taking Into Consideration Skin Pigmentation, Race and Ethnicity Docket No. FDA-2023-N-4976

On behalf of the American Association for Respiratory Care (AARC), thank you for accepting our comments on the FDA discussion paper *Approach for Improving the Performance Evaluation of Pulse Oximeter Devices Taking Into Consideration Skin Pigmentation, Race and Ethnicity.* We understand that the agency will hold a public meeting on February 2, 2024, and we are submitting our comments in advance of that meeting so that our voice may be heard by the Committee prior to their open discussions.

The American Association for Respiratory Care is a national professional organization with a membership of over 40,000 respiratory therapists who treat patients with acute and chronic respiratory diseases such as chronic obstructive pulmonary disease (COPD) and asthma. Through our advocacy, we support more than 170,000 practicing respiratory therapists across the country.

Respiratory therapists are an integral part of the healthcare system, providing care for patients with a myriad of pulmonary diseases, including chronic obstructive pulmonary disease (COPD), asthma, bronchitis, emphysema, cystic fibrosis, and acute respiratory distress syndrome. We also provide therapy for patients suffering from neuromuscular diseases, including Parkinson's disease, amyotrophic lateral sclerosis, and sleep apnea. Finally, we provide care for patients suffering from trauma and provide support for premature infants. We treat patients of all ages and are trained in pulmonary medicine to provide therapeutic care for patients suffering from pulmonary disease or conditions that impair breathing.

Background:
The FDA's Center for Devices and Radiological Health (CDRH) is seeking feedback on the discussion draft paper to improve the "quality of premarket studies and associated methods used to evaluate the performance of pulse oximeters taking into consideration a patient's skin pigmentation, and patient-reported race and ethnicity." With the release of this paper, the agency has requested input on specific topics to address how levels of oxygen saturation measurements may vary when taking into consideration a patient's skin pigmentation, race, and ethnicity. The indirect measure (SpO_2) of arterial blood saturation (SaO_2) is obtained using a pulse oximeter, and there is concern that the level of pigmentation of a patient's skin provides variably in measurement that has real-world implications for patient care that may lead to delays in escalation of care, failure to qualify patients for life-extending home oxygen therapy, incorrect or missed diagnoses. The following is the AARC response to the topics and questions as outlined in the discussion draft paper.

Clinical Study Design:
The AARC believes that changes are needed to allow for accurate measurement of SpO_2 in all skin tones. There is long standing belief and evidence to support that differences in skin pigment produce oxygen saturation measurements that are not accurate.[1] Meaning that there is wide variation when SpO_2 levels are compared to SaO_2 levels on the same patient within the same time frame. Often, particularly for individuals with darker skin tones, the measured level of SpO_2 is higher than when measured using SaO_2; these differences may have profound effects on healthcare decisions made by respiratory therapists, practitioners, insurance carriers, durable medical equipment providers, and the Medicare & Medicaid programs. Medical and treatment decisions affected by oxygen saturation levels include many medical situations, too numerous to name all of them here, but examples include adjusting oxygen levels and airway pressures for patients in the intensive care unit, treatment plan adjustments in respiratory therapy care, allowance of home oxygen for patients suffering from COPD, and other healthcare services that require accurate oxygen level measurement.

Also of importance is that incorrect levels of oxygen saturation may also lead to healthcare disparities and access to care issues. For example, we know that oxygen saturation levels are often overestimated in people with darker-pigmented skin, leading to missed diagnoses of hypoxemia.[2] These missed diagnoses may often occur in people who are already underserved due to factors associated with social determinants of health. The lack of accurate pulse oximetry readings further exacerbates healthcare disparities in many ways, including denial of access to home oxygen therapy when needed. The Biden administration has placed health equity and access to care at the top of its priority list since President Biden took office. The Equity Action Plan promulgated by the US Department of Health and Human Services outlined the administration's efforts to ensure appropriate and equal access to care. We believe that accurate measurement of oxygen saturation that accounts for differences in skin pigmentation is an important component in delivering equitable, accessible care.

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[1] Olubunmi, E.O. et al. *Pulse Oximeter Performance, Racial Inequity, and the Work Ahead*. Respiratory Care, Feb. 2022. Vol. 67, no. 2, pgs. 252-257.
[2] Ibid.

Recommendations:
The AARC recommends the FDA require the following to address the accuracy of measurement and to address the bias in pulse oximetry measurement among those with darkly pigmented skin tones. Our intention is to improve pulse oximetry accuracy, as accuracy is crucial for patient care.

1. Require that pulse oximetry device clinical trials be conducted in the environment in which they will be used. For example, pulse oximetry devices are used thousands of times every day in intensive care units around the country, but most, if not all, clinical trials are performed in a laboratory setting. Studies show that clinical trials performed in laboratory settings differ from clinical trials performed in the field.[3]
2. Clinical trial participants should match the diversity of the population. For example, as of 2020, approximately 60% of the US population is white, 19% is Hispanic or Latino and 12% are Black or African American.[4] A clinical trial should be designed with the same ratios applied to the trial cohort. Any clinical trial should also include the appropriate ratios for other populations including Asians and American Indian.
3. Require the use of the Monk Skin Tone test, Fitzpatrick score, or equivalent in all clinical trials. The need for data collection to be objective is emphasized here as most race information is self-reported.
4. Clinical trials should evaluate pulse oximeter measurements for various disease states, not only for healthy individuals in the laboratory setting.

In addition to our recommendations as noted above, AARC has provided answers to the specific questions as posed by the FDA in the discussion draft paper, and our answers provide additional detail to our clinical trial design recommendations.

Questions for Stakeholders:

1. Do you see benefits to conducting an initial assessment with the Monk Skin Tone (MST) scale to capture race and ethnicity diversity in pigmentation relevant to the US population followed with an objective Individual Typology Angle (ITA) assessment at the sensor site to assess non-disparate performance for enrolled participants?

   Yes, the AARC supports the use of a validated scale such as the MST scale and ITA across a range of skin pigments representative of the US population, as we noted above in our clinical trial recommendations. Integration of a skin pigment measure into the individual sensor would be welcome.

2. What are your thoughts on stratifying clinical study enrollment such that the entire range of skin pigmentation found in US race and ethnicity groups (i.e., the entire MST scale) is represented?

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[3] Foglia EE, Whyte RK, Chaudhary A, Mott A, Chen J, Propert KJ, et al. *The effect of skin pigmentation on the accuracy of pulse oximetry in infants with hypoxemia*. J Pediatr 2017;182:375-377. e2.
[4] United States Census Bureau. https://www.census.gov/library/stories/2021/08/2020-united-states-population-more-racially-ethnically-diverse-than-2010.html. Accessed Jan. 11, 2024.

The AARC supports the use of clinical trials that require a representative population, whether performed here in the US or elsewhere. We would note, however, that testing in healthy, laboratory-based volunteers alone might not provide the full story. Study enrollment of human subjects in the clinical environment may be necessary. For instance, mechanically ventilated patients in the ICU with altered perfusion and patients with COPD being assessed for home oxygen therapy. These are confounders and not easily controlled or matched, but assessment of the accuracy in patients where the devices will be used seems prudent.

3. Do you agree with the proposed definition of non-disparate performance assurance that the estimated maximum absolute difference in SpO2 bias across both ITA and MST levels is < 1.5% for SaO2 > 85%, and < 3.5% when 70% < SaO2 ≤ 85%?

   The AARC supports the proposed definition of non-disparate performance assurance but preface with noting that these are admirable and ambitious goals. The previous use of the accuracy root mean square metric was unclear to clinicians and was often interpreted as absolute accuracy.[5] Improving oximetry accuracy beyond historical performance is necessary.

4. What are your thoughts on using the proposed ITA-derived performance analysis and MST derived performance analysis to assess whether the criteria for non-disparate performance assurance are met across skin pigmentation, race, and ethnicity?
   Ideally, the performance analysis would use a method that is objective. The use of a skin tone measurement that is based on visual observation is subject to human error and external lighting. Several clinical sites have begun to use the Monk scale by holding a placard with the scale and trying to match the printed color to the patients skin tone at several sites on the body. This approach to measurement is subjective, and therefore we support the use of ITA-derived performance analysis.

5. Do you agree that the proposed approach for the clinical trial design achieves adequate race and ethnic diversity in enrolled participants to demonstrate reliable and accurate MST-derived performance analysis?

   Yes. The AARC supports the clinical trial design as proposed and suggests that our recommendations also be considered as the FDA developed final guidance.

6. In addition to what has been discussed, what are other ways for the Agency to improve evaluation of the performance of pulse oximeters, while taking into consideration differences in skin pigmentation?

[5] Hess, D. R. Using SpO_2: *Not as Simple as It Seems.* Respiratory Care, May 2023, vol. 68, no. 5.

As we have noted throughout, clinical trials should include enrollment of patients with the diseases and in the clinical scenarios where pulse oximeters are commonly used. Accuracy under conditions in the laboratory is well controlled and repeatable and is not an ideal way to study the measurements and outcomes of pulse oximeters. Given the very nature of the types of care that respiratory therapists provide, we believe pulse oximetry clinical trials must be performed under the conditions and in situations that represent how we practice in the field.

7. In addition to what has been discussed, what are other ways for the Agency to consider how race and ethnicity may impact the performance of a pulse oximeter's measurement of oxygen saturation?

   There is data that suggests skin pigment, perfusion, and device manufacturer each result in inherent bias. The use of a skin tone score like the MST scale should be used during validation of pulse oximetry devices. Additionally, we believe that the design evolution of pulse oximeters could include a measurement of skin tone using the light sources already present in the oxygen sensors, which would allow a nonbiased measurement of skin tone. Achieving design changes within pulse oximetry devices, such as use of the ITA to account for skin tone using the light source already present in the measurement device will require additional clinical trials.

The AARC thanks the FDA for its work thus far on improving pulse oximeter devices to account for differences in skin pigmentation, race, and ethnicity. If the agency would like to meet with us to discuss our recommendations, or if you have questions, please contact Miriam O'Day, Senior Vice President of Government Affairs, AARC (Miriam.oday@aarc.org).

Sincerely,

Carl Hinkson, MSc, RRT
AARC President, 2023 - 2024