SUMMARY MINUTES

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

Anesthesiology and Respiratory Therapy Devices Panel Meeting
Pulse Oximeters 2

February 2, 2024

9:00 a.m. EST

Webcast via Zoom

Attendees:

Chairperson
Hugh A. Cassiere, M.D., F.C.C.P., F.A.C.P.
Director Critical Care
South Shore University Hospital — Bay Shore, NY

Voting Members
Lonny B. Yarmus, D.O., M.B.A.
Professor of Medicine
Division of Pulmonary and Critical Care Medicine
Johns Hopkins University School of Medicine — Baltimore, MD

Naresh M. Punjabi, M.D., Ph.D.
Mary Jane and Lino Sertel Professor of Pulmonary Medicine, Chief
Division of Pulmonary, Critical Care, and Sleep Medicine
University of Miami Miller School of Medicine — San Francisco, CA

Anne Whitney Brown, M.D.
Transplant Pulmonologist
Inova Fairfax Advanced Lung Disease and Transplant Program
Senior Director of Clinical Affairs
Cystic Fibrosis Foundation — Falls Church, VA

Cheryl K. Gooden, M.D.
Associate Professor of Anesthesiology and Pediatrics
Yale School of Medicine — New Haven, CT

Temporary Non-Voting Members
Ben Saville, Ph.D.
President & Lead Statistical Scientist
Adaptix Trials, LLC — Austin, TX

Karla V. Ballman, Ph.D.
Consultant, Division of Clinical Trials & Biostatistics
Professor of Biostatistics, Mayo Clinic College of Medicine and Science
Associate Director of Quantitative Health Sciences, Mayo Clinic Comprehensive Cancer Center
Director, MCCCC Biostatistics Shared Resource — Rochester, MN

Raymond J. Lanzafame, M.D., M.B.A.
General Surgeon — Rochester, NY

James S. Taylor, M.D.
Clinical Professor of Dermatology
Cleveland Clinic Lerner College of Medicine of Case
Western Reserve University — Cleveland, OH

Tamorah R. Lewis, M.D., Ph.D.
Associate Professor Department of Pediatrics
Divisions of Neonatology and Pediatric Clinical Pharmacology
University of Toronto — Toronto, Ontario, Canada

Thomas E. Wiswell, M.D.
Neonatologist
Kaiser Permanente Moanalua Medical Center — Honolulu, HI

Julian M. Goldman, M.D., FASA
Anesthesiologist
Department of Anesthesia, Critical Care and Pain Medicine
Massachusetts General Hospital — Boston, MA

Jeffrey M. Feldman, M.D., MSE
Professor of Clinical Anesthesiology and Critical Care
University of Pennsylvania School of Medicine — Philadelphia, PA

Industry Representative
Wilson C. Wilson, M.D., M.A.
Executive Vice President Clinical Operations
Masimo Corporation — Irvine, CA

Consumer Representative
Rachel Brummert, M.S.
Communications Lead
American Society of Pharmacovigilance — Charlotte, NC

Patient Representative
Joseph P. O'Brien, M.B.A.
President & CEO
National Scoliosis Foundation
Patient Representative — Stoughton, MA

Food and Drug Administration
Malvina B. Eydelman, M.D., Ph.D.
Food and Drug Administration CDRH/OPEQ/OHTI
Office Director — Silver Spring, MD

James J. Lee, Ph.D.
Food and Drug Administration CDRH/OPEQ/OHTI/DHTIC
Division Director — Silver Spring, MD

Candace Nalls
Food and Drug Administration
Designated Federal Officer — Silver Spring, MD

CALL TO ORDER

Dr. Cassiere called the meeting to order at 9:00 a.m. He noted the presence of a quorum and stated that present members have received training in FDA device law and regulations, and stated the purpose of the meeting was to discuss an approach to improve quality premarket studies and associated methods used to evaluate the performance of pulse oximeters submitted for premarket review, taking into consideration the patient's skin pigmentation and patient reported race and ethnicity

Dr. Cassiere reminded the public and panelists that this is a non-voting meeting. He then asked members of the Committee and the FDA Staff to introduce themselves.

CONFLICT OF INTEREST STATEMENT

Candace Nalls, Designated Federal Officer, stated The agenda for today's meeting includes discussions on ongoing concerns regarding the accuracy of pulse oximeters in individuals with darker skin pigmentation. The advisory panel will explore approaches to enhance the quality of premarket studies and evaluation methods for pulse oximeters, considering the patient's skin pigmentation and reported race and ethnicity. Additionally, the committee will discuss the data manufacturers should provide to the FDA for evaluating pulse oximeters submitted for premarket review, covering both prescription and over-the-counter indications, as well as labeling considerations. She reported that a conflict-of-interest waiver was issued to Dr. Jeffrey Feldman. She announced that Dr. William Wilson would serve as the Industry Representative.

Ms. Nalls stated that during the anesthesiology and respiratory therapy devices panel meeting on February 2nd, 2024, Tamorah R. Lewis, MD, served as a temporary non-voting member. Dr. Lewis is a consultant to the Pediatric Advisory Committee in the Office of Pediatric Therapeutics, Office of the Commissioner. As a special government employee, Dr. Lewis underwent the customary conflict of interest review and reviewed the meeting materials. The appointment was authorized by Rachel Bressler, Acting Director of the Advisory Committee Oversight and Management Staff, on January 4th, 2024

GENERAL ANNOUNCEMENTS

Ms. Nalls made general announcements before handing the meeting back to Dr. Cassiere. She emphasized the importance of speakers identifying themselves each time they speak to assist the transcriber and stated the press contact is Carly Kempler.

FDA OPENNG REMARKS

Dr. Shuren opened a virtual public meeting of the Anesthesiology and Respiratory Therapy Devices Panel, emphasizing the significance of pulse oximetry as a public health tool and its disparate performance across different skin pigmentations and racial and ethnic groups. He highlighted the importance of improving premarket studies and evaluation methods for pulse oximeters, especially considering skin pigmentation and patient-reported race and ethnicity. The discussion aimed at refining data requirements for FDA evaluation and ensuring safe and effective use for all patients. The FDA has prioritized health equity and taken steps to enhance pulse oximeter accuracy across all U.S. demographics, informed by advisory meetings and real-world evidence studies. The FDA seeks feedback to update its Pulse Oximetry Guidance and continues to inform the public about pulse oximeter accuracy and limitations, thanking the Advisory Committee for their contributions and looking forward to their feedback.

Dr. Lee, Acting Director for the Office of Minority Health and Health Equity, emphasized the importance of understanding the relationship between race, ethnicity, skin pigmentation, and oximeter accuracy to advance health equity and address disparities among racial and ethnic minority populations. She highlighted the FDA's efforts across various initiatives to promote diversity in clinical trials, increase research on diverse groups, and enhance communication with diverse stakeholders to understand their perspectives and needs. Dr. Lee stressed the significance of integrating race and ethnicity data in evaluating health outcomes and the performance of medical devices, including pulse oximeters, to ensure their effectiveness and safety across all populations. The ongoing discussion on pulse oximeter performance and considerations for over-the-counter use is crucial for the FDA's regulation of these devices, with a focus on advancing health equity and preventing unintended consequences for all populations.

FDA PRESENTATIONS

Dr. Lee, presented on the FDA's regulation of pulse oximeters, highlighting their essential role in measuring arterial oxygen saturation (SpO2) as an alternative to direct arterial blood sampling (SaO2). He explained the principles of pulse oximetry, including the use of optical techniques and the significance of pulsatile arterial signals in determining oxygen saturation levels. The COVID-19 pandemic has increased the usage of pulse oximeters in both clinical and home settings.

Pulse oximeters, classified as moderate-risk devices, undergo FDA review through the 510(k) program based on substantial equivalence to existing devices. Clinical and bench testing, along with adherence to internationally recognized standards, are critical in evaluating their safety and effectiveness. The FDA guidance focuses on the use of updated consensus standards for oximeter validation.

Dr. Lee discussed the labeling of pulse oximeters for medical purposes, intended for trending or spot-checking oxygen saturation levels in clinical settings, and how certain devices are exempt from premarket review when intended for general wellness, not medical purposes. He also addressed the limitations of pulse oximetry, including the impact of skin pigmentation, patient dispositions, and other factors such as tattoos or nail polish, on accuracy. An update on adverse event reports related to pulse oximeters was provided, indicating most reports classified as malfunctions, with a small percentage related to serious injuries or deaths, underscoring the importance of understanding the limitations and clinical implications of pulse oximetry measurements.

Dr. O'Neill, Associate Director for Post-market Surveillance, presented a systematic literature review on the real-world performance of pulse oximeters, focusing on their accuracy across different skin pigmentations. She highlighted that the FDA has been aware of the potential impact of skin pigmentation on oximeter accuracy and recommended in 2013 that premarket studies include diverse skin pigmentation. Increased awareness during the COVID-19 pandemic, especially after a study showed Black ICU patients had higher rates of undetected hypoxemia compared to white patients, spurred further research and FDA action.

Real-world studies often relied on self-reported race and ethnicity and showed significant associations between race and oximeter accuracy, including potential impacts on clinical outcomes. **Dr. O'Neill** outlined the limitations of the studies, such as varying definitions of hypoxemia, the non-simultaneous nature of SaO2 and SpO2 measurements, and the inherent variability in real-world populations compared to controlled lab conditions. She also noted the heterogeneity of technology used and the potential for publication bias.

Despite these limitations, the evidence suggests that pulse oximeter accuracy varies by skin pigmentation, with recent studies continuing to explore this issue.

Dr. Hendrix, an anesthesiologist and the OHT1 Chief Medical Officer within OPEQ CDRH, outlined the FDA's proposed approach to enhance premarket clinical studies for pulse oximeters. She detailed the current premarket study requirements, emphasizing in vivo desaturation testing under laboratory conditions to verify pulse oximeter accuracy against the gold standard of blood oxygen saturation (SaO2) measurements.

The FDA's new approach aims to address the non-disparate performance of pulse oximeters, focusing on increasing the diversity and size of study participants, improving overall accuracy, and ensuring non-disparate performance across different skin pigmentation. **Dr. Hendrix** recommended increasing the minimum sample size from ten to 24 participants and including a broader range of skin pigmentation by evaluating both subjective and objective pigmentation methods.

The FDA proposes using the Monk Skin Tone (MST) scale for subjective assessment and the Individual Typology Angle (ITA) for objective measurement of skin pigmentation. This two-tiered approach aims to ensure an even spread of participants across the pigmentation spectrum and assess non-disparate performance accurately. The FDA also suggests tightening the accuracy requirements for pulse oximeters, with a proposed true population ARMS

Dr. Hendrix introduced a co-primary analysis for non-disparate performance, specifying performance goals for absolute differences in SpO2 bias across ITA and MST levels. The FDA aims to include diverse racial and ethnic groups in premarket studies to address potential disparities in pulse oximeter performance. The FDA recommended additional analyses for non-disparate performance at clinically relevant SaO2 thresholds. The proposed approach includes the same premarket clinical study design and evaluation criteria for over-the-counter pulse oximeters intended for medical purposes as for prescription use devices.

Dr. Pfefer discussed the impact of skin pigmentation on pulse oximetry accuracy, emphasizing the need for objective and subjective methods to assess skin pigmentation in pulse oximetry studies. He noted that melanin, mainly located in the epidermis, significantly absorbs light, affecting the performance of pulse oximeters. **Dr. Pfefer** highlighted several methods for assessing skin pigmentation, including subjective approaches like racial/ethnic self-identification and the Fitzpatrick scale, as well as objective methods using spectroscopy and colorimetry. He emphasized colorimetry as the most widely used approach, explaining how the CIE Lab color space and the Individual Typology Angle (ITA) quantify pigmentation.

Dr. Pennello then provided insights into the statistical assessment of pulse oximeter performance, focusing on accuracy, non-disparate performance assurance, and other objectives. He introduced concepts like SpO2 bias and imprecision, described various plots for data analysis, and discussed the importance of root mean square error (ARMS) as a primary performance measure. **Dr. Pennello** proposed co-primary analyses to ensure less than 3% ARMS and to demonstrate non-disparate performance across skin pigmentation levels, using ITA and MST. He also touched on potential study objectives, including the diagnostic accuracy of SpO2 for detecting conditions like hypoxemia and the use of ROC curves and inverse prediction to evaluate pulse oximeter performance and uncertainty.

QUESTIONS FROM THE COMMITTEE

Dr. Saville asked whether the points plotted on the graph represented the means of individual observations and sought clarification on the criteria used to define the maximum and

minimum range of the ITA. **Dr. Pennello** confirmed that the plot in question indeed represents the mean difference for each subject plotted against their Individual Typology Angle (ITA) value.

Dr. Goldman inquired for clarification from the FDA on the broad topics discussed during the session. **Dr. Eydelman** responded and stated that the FDA's primary objective is to maximize both performance and process symmetry for all patients in the United States. To achieve this goal, the FDA is actively seeking information from various sources, including input from the day's panel discussion.

Ms. Brummert questioned where the sample size of 24 participants came from and why the number is so low. Dr. **Gene Pennello** elaborated on the process and noted that sample size calculations led to the selection of 24 subjects, as this number provides the necessary power for evaluating pulse oximeters that are expected to have an ARMS of 2.5% or less.

Dr. Taylor raised a question regarding the composition of both medical and wellness devices, specifically asking if the FDA provides criteria for these devices and what type of composition information manufacturers must submit to the FDA.

Dr. Saville raised two follow-up questions, first, he inquired about the assumptions related to the subject variance used in the power calculations, he questioned whether the power calculation depended on this variance and if such details would be communicated to companies for clarity on expectations. **Dr. Pennello** confirmed that the sample size of 24 for pulse oximeter evaluations depends on between- and within-subject variances, as well as the bias.

Dr. Lanzafame inquired about whether similar calculations to those discussed for finger-based measurements in pulse oximetry studies are also made for other measurement sites, such as the earlobe. He questioned how the thickness of different measurement sites affects the data collected. **Dr. Cassiere** asked to hold that question for the Panel Discussions.

Dr. Wilson referred to the November 2022 meeting, noting a recommendation to decrease the ARMS in pulse oximetry studies. **Dr. Wilson** sought clarification from the FDA on whether there is still a recommendation to reduce the ARMS from 3% to 2% or 2.1%. **Dr. Pennello** responded that the previous requirement for pulse oximeters was for the point estimate of ARMS to be less than 3%, but now it must also meet this criterion with statistical significance. For practical purposes, the true ARMS would need to be around 2.5% or potentially as low as 2.1% to achieve 80% power for showing it is less than 3% with statistical significance.

GUEST SPEAKER PRESENTATIONS

MST Scale Pigmentation

Dr. Monk, emphasized the significance of skin tone in medical device performance, highlighting his research on colorism—a form of discrimination based on skin lightness or darkness. He noted the distinctiveness of skin tone from race and ethnicity and its association with various inequalities. Monk criticized the reliance on the Fitzpatrick scale for skin tone classification in medical studies, including pulse oximetry, due to its limitations and lack of representativeness. He introduced the Monk Skin Tone Scale, an alternative he developed to more accurately measure skin tone diversity. This scale has been validated through extensive research and adopted by organizations like Google and Meta.ai for its inclusiveness and ease of use. Monk advocated for the combination of subjective and objective measures of skin tone in research to better understand its impact on medical device accuracy, including pulse oximetry, and to address broader social determinants of health.

Real-World Evidence in Pulse Oximetry

Dr. Bickler provided an update on the EquiOx study, a prospective clinical investigation of pulse oximeter errors in hospitalized patients, after enrolling about 480 participants. Conducted at the University of California, San Francisco, and supported by CERSI and the FDA, the study aims to measure the bias in pulse oximeter SpO2 readings across various skin pigmentations among critically ill hypoxemic patients. The secondary objectives include comparing subjective skin pigment scales with objective spectrophotometer data, examining the relationship between skin pigmentation and race among San Francisco hospitalized patients, investigating if race-related bias differences are due to skin pigmentation, assessing if clinical pulse oximeter performance aligns with controlled lab studies, and exploring low perfusion as a potential factor in performance disparity.

The EquiOx study was initiated in response to 2020 reports of occult hypoxemia, particularly in black patients, where pulse oximeter readings inaccurately indicated normal oxygen levels. The study addresses challenges faced by previous research, such as imprecise pairing of SpO2 and SaO2 measurements and the absence of skin pigmentation data

Dr. Hendrickson presented an update on patient enrollment for the EquiOx study, highlighting the diversity of self-identified racial categories from the electronic medical records, including a significant proportion of patients identifying as "other race." The use of the Monk Skin Tone Scale revealed a concentration of participants with mid-range skin tones, with fewer participants at the extremes, especially in the darkest categories labeled I and J.

The distribution across the Monk Skin Tone categories showed overlapping skin pigmentation across different racial identities, though the darkest categories, H and I, were predominantly comprised of individuals self-identifying as black or African American. **Dr. Hendrickson** also discussed the limitations of the Fitzpatrick skin tone group as an imprecise method for categorizing skin pigmentation, evidenced by the broad overlap in ITA measurements across all Fitzpatrick groups. The study also highlighted the importance of the perfusion index, with data suggesting that a perfusion index of one or less was associated with missed hypoxemia. Most pulse oximeter readings were taken from fingers, though other locations like the ear were used if necessary.

Dr. Almond presented a prospective clinical study assessing the accuracy of pulse oximeters in pediatric patients with increased skin pigmentation. The study aims to address the systematic overestimation of oxygen saturation by pulse oximetry in children with darker skin, potentially leading to missed critical hypoxemia.

The study design includes a multicenter approach, involving not-anemic children under 21 with arterial lines, primarily in children's hospitals' cardiac cath labs and ICUs. Skin pigmentation is measured using various scales, including the evolution scale, the Monk Skin test, and the Fitzpatrick scale, alongside colorimetry using Konica and Delfin colorimeters. The primary outcome focuses on the difference between SpO2 and SaO2, with secondary variables including perfusion index, age, saturation, and self-reported ethnicity. Preliminary findings suggest a moderate correlation between the Monk Skin Tone test, other pigment scales, and ITA.

Patient Perspectives: - Adult

Mr. McClure shared his personal experience with using a pulse oximeter as part of his management for emphysema, a severe form of COPD. Diagnosed in 2013 and having quit smoking in 2019, he underwent lung valve surgery in 2020, which led to his pulmonologist

prescribing 24/7 oxygen therapy in 2021. Initially, he used a pulse oximeter gifted by an acquaintance, but found it slow, difficult to read, and not user-friendly. Eventually, he purchased a better model from Amazon, which, despite being easier to read, still occasionally provided inaccurate readings, particularly concerning given his melanated skin, a factor he learned could affect accuracy from his daughter. Mr. McClure expressed concern about the general lack of awareness among medical professionals regarding the inaccuracies of pulse oximeters for individuals with melanated skin, except for his African American primary care physician. He highlighted the importance of improving pulse oximeter technology to ensure safety for all patients, indicating a broader issue of racial disparities in medical device performance.

Patient Perspectives: - Pediatric

Ms. Ryan Jolly shared her experience with using pulse oximeters for her African American daughter, who has been utilizing the device for ten years due to various medical conditions related to a rare chromosomal abnormality. Despite her nursing background, **Ms. Jolly** faced challenges with the pulse oximeters, particularly noting inconsistencies in readings for her darker-skinned daughter compared to her paler child. She observed that the devices often lose readings without apparent cause and highlighted the difficulty in understanding the device's icon-based alerts without a medical background.

Ms. Jolly also discussed the evolution of her daughter's pulse oximeter use, including adjusting alarm settings in consultation with their pulmonologist as her daughter aged. She emphasized the crucial role the pulse oximeter plays in allowing her daughter to live at home and providing their family with a sense of normalcy, despite the need for constant medical supervision.

Patient Perspectives: - Industry

Ms. Tara Federici, Vice President of Technology and Regulatory Affairs for AdvaMed, highlighted the association's commitment to improving diversity in medical device studies and advocated for more inclusive clinical trials. AdvaMed, representing over 400 member companies, works towards creating a favorable environment for global healthcare innovation and access. **Ms. Federici** emphasized AdvaMed's support for diversifying clinical trials, mentioning specific initiatives like the health equity initiative and the Take Her Health to Heart initiative aimed at increasing the enrollment and retention of women in cardiovascular trials.

Dr. Stephen J. Barker, Professor Emeritus of Anesthesiology at the University of Arizona and Chief Science Officer at Masimo, provided an industry perspective on the FDA's discussion on skin pigmentation's impact on pulse oximetry. He commended the FDA and industry's alignment on the importance of medical device performance equity. Barker discussed the FDA's request for feedback on improving pulse oximeter evaluations, particularly concerning skin pigmentation diversity. **Dr. Barker** recommended stratifying skin pigments into three MST cohorts to detect performance differences and stressed the need for including a diverse range of skin tones in studies. He proposed tightening the SpO2 accuracy requirements from a 3% Average Root Mean Square to a 2% ARMS and applying these standards to reprocessed sensors.

PANEL DELIBERATIONS

Dr. Feldman asked **Dr. Barker** about his recommendation to measure skin pigmentation at sites such as the back of the hand, which are not typical locations for applying pulse oximeter sensors. Dr. Feldman asked what the implications of this approach might be. Dr. Barker

responded that the fingertip's skin absorbance varies significantly between different fingers and does not accurately represent the rest of the hand's skin pigmentation.

Dr. Lewis asked the two patient representatives, to elaborate on the significance of not only the momentary accuracy of pulse oximetry readings but also the time it takes for the device to display an accurate reading upon application and its ability to sustain accurate readings over extended periods.

Dr. Lewis asked **Mr. McClure** and **Ms. Jolly**, the significance of not only the momentary accuracy of pulse oximetry readings but also the time it takes for the device to display an accurate reading upon application and its ability to sustain accurate readings over extended periods. **Ms. Jolly** responded that is mostly impacted sleep and quality of life. **Dr. Lewis clarified** that pulse oximeters need to be accurate for 30-60 minutes. **Ms. Jolly** agreed. **Mr. McClure** stated he needs the Pulse oximeters to be able to give a quick accurate reading.

Dr. Ballman raised a question about the study design, noting that while it is adequately powered for 24 patients overall, it might not be sufficiently powered for six patients in each individual category.

Dr. Eydelman facilitated responses to earlier unanswered questions, with **Dr. Hendricks** and **Dr. Pennello** providing detailed explanations. **Dr. Hendricks** addressed a question regarding sensor placement and the chosen methodology for pigmentation measurement, explaining that the wide pigmentation range of the forehead was considered to ensure enrollment across all skin pigmentation ranges. **Dr. Hendricks** also explained the rationale behind the acceptance criteria of 1.5% and 3.5% for non-disparate bias performance, which were based on the limits of current technology and clinical relevance.

Dr. Lewis inquired about the consideration of variations in local blood flow in premarket study recommendations for pulse oximeters, given its significant interaction with skin pigmentation. **Dr. Hendrix** responded, explaining that the FDA is aware of the influence of percent modulation or perfusion index on pulse oximeter performance. The FDA is reviewing real-world studies to better understand the impact of perfusion variation across different skin pigmentations. **Dr. Weininger** added that efforts to address the issue include experimental methods like cooling one side of the body and using a simulator to adjust red and infrared light balance and lower percent modulation, both of which are complex and yet to be validated.

Dr. Feldman underscored the importance of addressing the influence of race, ethnicity, and specifically skin tone on pulse oximeter performance, expressing concerns whether the proposed requirements would conclusively resolve these questions. **Dr. Feldman** questioned the adequacy of the proposed patient population definitions, noting that a total sample size of 24 and subgroups of six to nine patients seemed small.

Dr. Lanzafame raised questions regarding real-world performance factors that may affect pulse oximeter accuracy, and inquired whether study designs that permit hand warming also consider the time course of optical component shifts and the tissue thickness where measurements are taken. **Dr. Eydelman** explained that desaturation lab studies typically last about two hours, allowing for stable measurements at various oxygen saturation levels. However, she acknowledged that this might not account for all real-world conditions, such as physiological differences or how clinicians might reposition the oximeter for better readings.

Dr. Goldman had concerns about the proposed acceptance criterion and its potential market impact, particularly on the availability of lower-cost pulse oximeters during public health emergencies like the COVID-19 pandemic. **Dr. Eydelman** responded by inviting panel input on

these topics to inform the FDA's future direction, agreeing with the need for a cautious approach to avoid unintended consequences.

Dr. Wilson emphasized the importance of capturing pulse oximetry measurements across a broader range of oxygen saturation levels, particularly between 70 and 90%, to reflect its dynamic nature in real-world settings.

Dr. Yarmus and **Dr. Cassiere** discussed the importance and feasibility of incorporating real-world data into pulse oximetry research, especially in ICU settings.

Dr. Saville raised concerns about the analytical approach to evaluating pulse oximeter accuracy, suggesting a prediction model where arterial oxygen saturation is the endpoint predicted from pulse oximeter readings and other covariates. **Dr. Pennello** responded, that the challenges of modeling SaO2 as the dependent variable with SpO2 as a predictor due to measurement errors in SpO2 that could distort parameter estimates.

Dr. Wilson elaborated on **Dr. Yarmus's** suggestion of utilizing ICU patients with preexisting arterial lines for pulse oximeter accuracy studies. He noted the challenge of obtaining adequate data for oxygen saturation levels below 90%, particularly in the 70 to 80 range, due to the clinical practice of quickly addressing low oxygen levels. **Dr. Cassiere** responded, clarifying that the concern is not about consistently low O2 saturation in ICU patients but about identifying occult hypoxemia in patients with low perfusion index, where the pulse oximetry reading may overestimate arterial saturation.

Dr. Feldman raised concerns about the current methods of skin tone assessment for pulse oximetry, highlighting that none of the existing methods, including the Individual Typology Angle (ITA), were developed with the specific purpose of evaluating how skin tone affects light transmission for pulse oximetry

Dr. Saville raised concerns about the statistical approach to non-disparate performance criteria in pulse oximetry, questioning the use of maximum model-based bias thresholds of 1.5% and 3.5%. Dr. Pennello acknowledged that the chosen thresholds were based on the statistical power achievable with a sample size of 24, reflecting the current technology limits.

Dr. Punjabi expressed concerns about the FDA's proposed acceptance criteria for non-disparate performance in pulse oximetry, specifically the 3.5% threshold. He highlighted the significant implications this criterion could have in the field of sleep and breathing, particularly in diagnosing sleep-disordered breathing, where a 3% desaturation is a key criterion for identifying the disease. **Dr. Hendricks** explained that the criteria were modeled based on data from well-performing pulse oximeters in desaturation lab studies, aiming to balance feasibility with clinical relevance.

Dr. Saville raised concerns about scenarios where a new pulse oximeter might meet general accuracy criteria but fail to meet criteria for non-disparate performance regarding skin pigmentation. He questioned how the FDA would interpret such outcomes, given they might not differ from current standards. **Dr. Eydelman** from the FDA responded by seeking recommendations from the panel, emphasizing the importance of transparent labeling for devices that reach the market.

OPEN PUBLIC HEARING

Dr. Sam Ajizian from Medtronic emphasized the company's commitment to enhancing pulse oximetry performance, acknowledging variables like skin pigmentation that affect device accuracy. Medtronic supports collaborative efforts with the FDA, industry, and healthcare

practitioners to advance pulse oximetry and ensure device accuracy for all patients, irrespective of skin pigmentation.

Dr. Ajizian agreed with most FDA recommendations, including increasing study sample sizes and incorporating validated scales for skin tone diversity, suggesting a tolerance of ±1 on the Monk Skin Tone Scale to aid patient enrollment. He recommended further research before setting performance thresholds for non-disparate bias, highlighting the importance of partnership in achieving health equity.

Dr. Michael Abrams from Public Citizen's Health Research Group highlighted ongoing concerns about the inaccuracies of pulse oximeters, particularly regarding their performance in individuals with darker skin pigmentation.

Dr. Abrams also noted that most applications for FDA clearance of pulse oximeters provide little information on the effects of race, ethnicity, or skin pigmentation, a trend confirmed by his review of recent FDA cleared applications. Despite the advisory committee's efforts and FDA communications warning about device inaccuracies, there has not been a noticeable increase in adverse event reports or recalls related to pulse oximeters, nor is race and ethnicity commonly reported in these events.

Dr. Scott Lucas, Vice President of Device Safety at ERSI, commends the FDA for addressing healthcare equity, specifically the performance disparity of pulse oximetry across different skin tones. ERSI supports the FDA's proposal to standardize skin pigmentation assessment in clinical trials for pulse oximeters, highlighting the importance of addressing human factors in these assessments. Lucas points out limitations in the proposed MST (subjective) and ITA (requires consistent colorimeter use) methodologies, recommending their combined use until a better understanding of potential disparities is achieved.

Dr. Grace Wickerson from the Federation of American Scientists emphasized the importance of considering a diverse range of participants in the design of clinical studies for pulse oximeters to ensure devices work well for all populations, particularly marginalized groups like Black and Brown Americans. They highlighted the need for evidence-based thresholds to prevent bias and recommended reviewing devices post-market to detect performance in clinical environments, suggesting a collaboration with the Veterans' Health Administration.

Dr. Ash Fawzy from Johns Hopkins University discussed the clinical consequences of racial bias in pulse oximetry, sharing strategies for gathering high-quality clinical data. During the COVID-19 pandemic, they observed systematic overestimation of oxygen saturation by pulse oximeters in Black and Hispanic patients, leading to delayed or denied COVID-19 treatment. Fawzy advocated for testing pulse oximeters on a diverse patient population using objective skin tone measurements and real-world clinical data to ensure equitable device performance.

QUESTIONS FROM PANEL

Ms. Brummert inquired if Medtronic considered a voluntary recall of their pulse oximeters due to faulty data related to skin pigmentation. **Dr. Ajizian** from Medtronic responded that their continuous quality and safety processes have not indicated a need for such actions. He stated that Medtronic's devices conform to current FDA standards, and objective data support their performance. **Dr. Ajizian** emphasized the importance of pulse oximeters in critical care settings and mentioned Medtronic's focus on education regarding the devices' use, particularly in patients with dark pigmentation. He advised that pulse oximeter readings should be one factor in a comprehensive medical evaluation, indicating that the benefits of their products outweigh the discussed risks.

Dr. Lewis inquired about Medtronic's technological innovations in pulse oximetry, specifically regarding improvements for patients with dark skin pigmentation. **Dr. Ajizian** from Medtronic responded, highlighting that while he could not discuss proprietary information, the company has publicly shared recalculated internal data on pulse oximeter performance in light and dark-skinned subjects.

Dr. Cassiere expressed concern over **Dr. Ajizian's** previous remarks, perceiving them as potentially blaming the medical community for using pulse oximetry as a threshold for COVID-19 treatment. **Dr. Ajizian** clarified that the pandemic indeed pushed pulse oximetry into critical use for triaging overwhelmed emergency departments and home monitoring. He emphasized that medical training teaches that diagnostic tools like pulse oximeters should not be used in isolation but as part of a comprehensive assessment of the patient.

Dr. Goldman inquired about the causes of outlier readings in pulse oximeter data, as opposed to a homogenous bias, during Dr. Fawzy's presentation on pulse oximetry accuracy in darkly pigmented patients. **Dr. Fawzy** acknowledged the observation of variable pulse oximeter errors within the same patient at different times, citing research by **Dr. Valbuena**, which indicated fluctuating errors throughout the day. Despite attempts to control for variables like pH and mean arterial pressure, **Dr. Fawzy** highlighted the complex interactions affecting pulse oximeter accuracy that warrant further investigation. Additionally, **Dr. Fawzy** mentioned conducting a visual assessment of pulse oximeter tracing quality in their study, noting no significant difference in results when analyzing this factor. He emphasized the potential for more insightful research if pulse oximeter manufacturers provided access to raw data, which could enhance understanding of bias in clinical settings.

Dr. Gooden inquired about the impact of probe location on pulse oximeter accuracy, particularly in pediatrics where probes are often placed on the toe or foot, and how this affects pigmentation considerations. **Dr. Ajizian** from Nellcor responded by highlighting the importance of validating probe positions as per their instructions for use and acknowledged the variability in performance and positioning across different manufacturers. He emphasized the necessity for continuous education for providers to ensure correct probe placement and usage.

INVITED SPEAKERS

Dr. Joseph Wright, Chief Health Equity Officer at the American Academy of Pediatrics (AAP), emphasized the importance of designing and testing medical devices, including pulse oximeters, with the unique needs of children in mind. He highlighted the challenges in pediatric device development compared to advancements in pediatric drug development and called for more equitable study of medical devices in children. **Dr. Wright** noted children's anatomical and physiological differences from adults, emphasizing the necessity of specific research in pediatric populations, including neonates and children with conditions like cyanotic congenital heart disease. He acknowledged incremental progress in understanding pulse oximetry's performance in children but stressed that these efforts are only beginning. **Dr. Wright** urged the FDA to encourage companies to study their devices in children equivalently to adults, to avoid leaving pediatric needs behind.

Dr. Michael Lipnick discussed the OpenOximetry collaborative community, aimed at addressing the disparity in pulse oximeter performance across different skin pigments and improving global health equity. The initiative includes a prospective clinical trial supported by the FDA and studies at UCSF, focusing on enhancing pulse oximeters' performance for patients with darker skin. The collaborative community, comprising over 150 members from diverse

fields and 18 countries, aims to identify challenges, improve research and regulatory practices, promote data sharing, and advocate for equitable pulse oximeter performance. Subgroups within the community focus on clinical trials, education, skin color diversity, and data sharing to harmonize data collection, develop educational materials, ensure diversity in pulse oximeter studies, and leverage data to investigate performance issues.

Dr. Indira Gurubhagavatula from the American Academy of Sleep Medicine highlighted the critical role of oximetry in diagnosing sleep apnea and emphasized the need for high accuracy in oximeters, especially for patients with darker skin pigments. She pointed out that current oximetry technology may underestimate desaturations in these patients, affecting the diagnosis and management of sleep apnea. **Dr. Gurubhagavatula** stressed the importance of calibration studies that reflect the diversity of sleep center patients, including a wide spectrum of skin color, race, gender, and health conditions. She called for more inclusive calibration studies, post-market surveillance of devices, labeling that includes bias and variance metrics, and education for all stakeholders. The goal is to ensure oximeters can accurately detect desaturations with minimal error to prevent missed diagnoses and the severe consequences of untreated sleep apnea, which include increased risk of cardiovascular diseases, cognitive impairment, and accidents.

Dr. Aaron Dorian Baugh, an assistant professor of medicine at UCSF, spoke on the importance of addressing the performance of pulse oximeters across different skin tones. He supported the dual approach of using both the Monk Skin Tone scale and the Individual Typology Angle for assessing skin pigmentation's effect on oximeter accuracy. **Dr. Baugh** emphasized the dynamic nature of oximeter correlation with arterial blood gases, suggesting experimental replication of ICU conditions, like unwarmed hands or simulations of hypoperfusion, to better understand device performance. **Dr.Baugh** highlighted a public misunderstanding linking pulse oximeter inaccuracies predominantly with race, particularly Black individuals, and stressed the need for the FDA to clarify and address both the scientific hypotheses and public perceptions.

Dr. Ann Rizzo, representing the American College of Surgeons, addressed the FDA's proposal on pulse oximetry, highlighting the COVID-19 pandemic's revelation of inaccuracies in pulse oximetry, particularly in patients with darker skin. She noted that despite these inaccuracies, there was no evidence of differential treatment based on skin color. Rizzo acknowledged that pulse oximetry inaccuracies arise not only from skin color but also from factors like blood dyscrasias, tattoos, and external conditions such as temperature. She emphasized that physicians often verify oximetry readings with blood oxygen saturation tests to ensure accuracy, especially in critical cases.

Dr. Rizzo advocated for research into the correlation between skin color and pulse oximetry but urged the FDA to also invest in developing new technologies for more accurate, noninvasive oxygen saturation measurements. She suggested near-infrared spectroscopy as a promising alternative that is unaffected by skin color or thickness. Her statement supported the idea that while understanding the impact of skin tone on current pulse oximetry is important, the ultimate goal should be to innovate and improve the technology to overcome its inherent limitations.

Dr. Jesse Ehrenfeld, representing the American Medical Association, addressed concerns regarding the accuracy of pulse oximeters for patients with darker skin tones, highlighting that these devices are more likely to provide misleading readings for such individuals. This issue has led to missed critical diagnoses of low blood oxygen levels,

particularly highlighted during the COVID-19 pandemic. The AMA's recommendations include requiring quantitative data on device performance across a range of skin pigmentations in clinical studies and prioritizing devices with comparable performance across the skin tone spectrum on payer formularies. These measures aim to address systemic bias and racism, advocating for health equity and ensuring high-quality care for every patient.

Dr. Nirav Bhakta, representing the American Thoracic Society (ATS) and faculty at the University of California in San Francisco, emphasized the importance of pulse oximeter accuracy for clinicians and investigators in pulmonary, critical care, and sleep medicine. He proposed five points for consideration: Evidence-based Authorization, Diverse Study Populations, Transparency, Post-Marketing Evaluation, and Regulation of Consumer-Grade Pulse Oximeters. Dr. Bhakta concluded by appreciating the FDA's efforts but urged for more rigorous standards, increased diversity in testing, and transparency in reporting.

Dr. Megan Lane-Fall, Vice President of the Anesthesia Patient Safety Foundation (APSF), provided a video commentary to the FDA Medical Devices Advisory Committee regarding pulse oximetry and skin pigmentation. They emphasize the importance of accurate pulse oximetry in clinical settings, where it informs crucial decisions in perioperative care, including surgery, supplemental oxygen administration, and patient admission decisions. The APSF calls for FDA adjustment of approval standards for pulse oximeters to ensure accurate performance across various skin pigmentation levels and clinically relevant oxygen saturation ranges. They argue against using race as a basis for subject selection in device testing studies, advocating instead for testing under conditions affecting pulse oximeter accuracy, such as perfusion.

Dr. Garrett Burnett, an anesthesiologist at the Icahn School of Medicine at Mount Sinai in New York City, presented on behalf of the Society for Technology in Anesthesia. He highlighted recent studies indicating errors in pulse oximeter readings related to skin pigmentation. Dr. Burnett emphasized the importance of equitable pre-market testing of pulse oximeters to ensure accuracy for all patients, supporting the panel's proposal to incorporate objective measures of skin pigmentation. He suggested linking the Monk Skin Tone Scale to ITA measurements to streamline testing. Dr. Burnett urged the FDA to provide research funds to support ongoing investigations into this issue. He thanked the panel and the FDA for their attention to the matter on behalf of himself and the Society for Technology and Anesthesia.

Dr. Terry Davis, President of the American Association of Critical Care Nurses (AACN), addressed the FDA on the issue of pulse oximetry accuracy and skin pigmentation. AACN, representing acute and critical care nurses, emphasized the importance of ensuring accurate readings for all patients. They acknowledged progress in raising awareness but emphasized the need for further action to address disparities. **Dr. Davis** highlighted AACN's commitment to bridging the gap in patient care, including providing educational webinars on pulse oximetry and skin color. Key points from the webinar emphasized the need for proper sensor placement and awareness of accuracy disparities in patients with darker skin pigmentation. AACN advocated for the development of processes to ensure pulse oximetry accuracy, including consumer-grade devices, and emphasized the importance of considering skin pigmentation in testing any technology.

FDA QUESTIONS TO THE PANEL

Question 1

Dr. Lanzafame expressed his view on the proposed approach by the FDA for clinical trial design regarding pulse oximeters. He acknowledged the advantages of using both the Monk Skin Tone (MST) and Individualized Topology Angle (ITA) approaches, along with gathering subjective information on race and ethnicity. However, he emphasized the importance of including a greater proportion of individuals with darker skin tones in the study population. Additionally, he raised concerns about the location of measurement, particularly mentioning that the Palmer aspect of the hand, where the sensor is placed, may introduce experimental variability. **Dr. Lanzafame** suggested considering multiple measurements over larger sites to obtain an average, acknowledging challenges related to the size of measurement devices.
Dr. Goldman expressed general support for the proposed approach of combining visual assessment with the Monk Skin Tone (MST) scale and objective assessment with the Individualized Topology Angle (ITA). He supported the idea of "binning" the MST categories, recognizing the challenge of finding sufficient patients in each MST slot and acknowledged the measurement of ITA on the dorsal aspect of the distal finger as a reasonable approach, despite it not being the actual measurement site for pulse oximetry.

Dr. Feldman emphasized the importance of addressing whether skin tone introduces bias in approved devices. While he agreed with including the Monk Skin Tone (MST) scale in the testing methods, he expressed concerns about the proposed sample sizes and testing methods. He noted that while the Individualized Topology Angle (ITA) provides an objective measure of skin pigmentation, it does not reveal how light interacts with the skin at the sensor site. He referenced a recent abstract from the Society for Technology and Anesthesia (STA) meeting, suggesting that analyzing the absorption of light by different skin tones might be a more effective approach.

Dr. Feldman suggested that simply measuring melanin content, as ITA does, might not provide sufficient information about how light is affected by skin pigmentation. He proposed that using the ITA measurement at locations other than the finger might not fully address the issue of skin tone and its interaction with pulse oximeter measurements.

Dr. Wilson supported the use of the Monk Scale as a subjective measure of skin pigmentation and suggested using the distal fingertip, on the dorsal aspect just proximal to the nail bed, as a surrogate for the ITA measurement. He recommended taking an average of three measurements at this site to account for potential variability. **Dr. Feldman** agreed that the Monk Scale covers the spectrum well and acknowledged the correlation between ITA and the Monk Skin Scale. However, he expressed concerns about the light pathway through the finger, which may have less pigment than the measured area. **Dr. Goldman** emphasized the importance of measuring the ITA close to the measurement site to assess the effect of skin pigment accurately. He suggested taking three measurements and averaging them to ensure consistency.

Dr. Taylor deferred to the technologists' expertise and emphasized the importance of considering comorbidities in the study design. He highlighted the need to address factors such as finger edema and sun exposure, particularly when assessing the forehead, which may be more susceptible to pigmentation from sun exposure. He suggested involving the Skin of Color Society, a group of dermatologists familiar with this issue, for additional insights. However, he clarified that while comorbidities should be considered, they may be more relevant in real-world testing rather than in studies involving healthy volunteers.

Dr. Lanzafame emphasized the importance of understanding the spectral curves for melanin and its variants, which dictate how light is absorbed and transmitted at different wavelengths. He clarified that the density of melanin at the specific measurement site is crucial for accurate pulse oximetry readings. **Dr. Lanzafame** acknowledged the efforts to address this

issue through measures like the Monk Skin Tone scale (MST) and Individual Typology Angle (ITA) but cautioned that there are other confounding factors to consider beyond skin pigmentation.

Dr. Gooden raised concerns regarding the inclusion of pediatric patients in the studies moving forward, particularly emphasizing the need to consider the placement of the pulse oximetry probe. She suggested that in pediatric patients, the probe is often placed on the toe or foot instead of the fingertip or forehead, which are commonly used in adults. **Dr. Gooden** urged the FDA to take this into account when designing studies involving pediatric patients.

Dr. Feldman clarified that the ultimate goal is to ensure that approved devices perform accurately regardless of skin tone or racial designation. While Monk's Skin Tone has some value, it may not fully represent what happens at the sensor site, thus the importance of measuring transmission of light at that location. **Dr. Feldman** suggested that measuring light transmission at specific frequencies and stratifying patients based on this measurement could provide more relevant and reliable results. He acknowledged that this approach is not currently established in the literature but emphasized the importance of exploring new methods to improve accuracy.

Dr. Brown expressed support for the inclusion of the Monk Skin Tone (MST) scale in the study design. She emphasized the importance of enriching the study population with a variety of MSTs, including extreme values like two and nine. **Dr. Brown** favored an approach that focused on observing how the devices perform in actual practice, suggesting that while objective measurements of light transmission are beneficial, ensuring a diverse sample size may be more crucial.

Dr. Wiswell expressed concern about the low number of participants (24) proposed for the study, considering they are healthy volunteers and not necessarily representative of future device users. He suggested increasing the sample size to ensure the study is adequately powered. Additionally, **Dr. Wiswell** proposed narrowing down the Monk Skin Tone (MST) scale into five buckets instead of three to capture a broader range of pigmentation levels, especially at the darker end of the spectrum. **Dr. Yarmus** agreed with **Dr. Brown's** approach and emphasized the need for separate observation studies in relevant clinical scenarios to complement the proposed clinical trial.

Dr. Lewis highlighted two crucial points. Firstly, she emphasized the importance of powering pre-market studies to detect between-group differences, especially across the full range of Monk Skin Tone categories for both adults and pediatric patients. This approach aims to regain trust among the public and clinicians by ensuring comprehensive evaluations. Secondly, **Dr. Lewis** suggested considering oversampling darker skin pigment groups that are at higher risk of poor performance. **Dr. Lewis** also questioned the adequacy of the current sample size of 24 volunteers for the study, suggesting that it may not be sufficient to detect between-group differences and advocating for a more robust sample size.

Dr. Saville discussed the importance of powering pre-market studies adequately to detect between-group differences, especially concerning skin pigmentation. He expressed concerns regarding the sample size of 24 volunteers, stating that it may not be sufficient to assess the interaction between skin pigmentation and bias in pulse oximetry accurately. **Dr. Saville** suggested that the current power calculations may be insufficient and recommends using virtual clinical trial simulations to inform the appropriate sample size. He emphasized the need for a nuanced approach to power calculations, considering various assumptions and scenarios**. Dr. Saville** suggested that increasing the sample size may mitigate some issues but stresses the

importance of understanding the sensitivity of power calculations to different assumptions. He effectively.

Dr. Feldman emphasized the importance of framing the research question appropriately in pre-market studies to address differences in pulse oximetry performance based on skin tone. He suggested that the goal should be to statistically demonstrate non-disparate performance across different skin tone groups within the specified accuracy range. **Dr. Feldman** also discussed the need for manufacturers to reevaluate device design to ensure accuracy across diverse skin tones.

Dr. Goldman emphasized the importance of exploring real-world phenomena that may impact pulse oximetry accuracy. **Dr. Feldman** agreed with this sentiment but cautions against incorporating real-world evidence into pre-market submissions due to the associated increase in cost and complexity. Both emphasized the value of ongoing prospective studies to gather information that can improve technology and patient care but advocate against including such evidence in regulatory submissions.

Question 2

Dr. Wiswell expressed concerns regarding the absolute difference in saturation levels allowed by the proposed criteria, particularly in patients with critical cardiac conditions or pulmonary hypertension. **Dr. Cassiere** inquired about the correlation of peripheral pulse oximetry with arterial blood gas levels, to which **Dr. Wiswell** explained that while correlation is attempted, it's not always feasible, especially in rapidly changing conditions. **Dr. Cassiere** acknowledged Dr. Wiswell's concerns.

Dr. Feldman raised a question regarding the terminology used in the criteria, suggesting that "ARMS" (accuracy root-mean-square) might be more appropriate than "bias" to encompass both bias and precision. **Dr. Pennello** clarified that bias was indeed the intended term, with co-primary objectives focusing on ARMS and non-disparate performance. **Dr. Feldman** expressed concern about the consistency between bias and ARMS requirements, prompting discussion about the differences in bias between skin color levels.

Dr. Hendrix explained the concept of SPO2 differences across skin tones, emphasizing the need for a continuum approach. **Dr. Cassiere** inquired about the 95% confidence interval's role in addressing precision concerns, and **Dr. Pennello** clarified its application in non-disparate performance assurance.

Dr. Saville expressed concerns regarding the criteria for non-disparate performance analysis, particularly the reliance on point estimates of bias between different skin tones. He suggested exploring confidence intervals and alternative methods like Bayesian probability to quantify disparate performance more effectively.

Dr. Goldman expressed concerns about the potential implications of applying pass-fail criteria across different skin pigmentation ranges in an evolving field. He emphasized the importance of disclosing performance limitations and suggested that current approaches might overlook valuable information provided by devices. **Dr. Goldman** questioned the use of pass-fail criteria without a thorough understanding of root causes and highlighted the need for more comprehensive evaluation methods.

Dr. Ballman made several comments regarding the understanding of disparate measures and the need for instruments to perform consistently across different skin tones and acknowledged the complexity of assessing bias between groups but emphasized the importance of ensuring instrument performance across all skin tones. **Dr. Ballman** expressed support for a

binary acceptance criterion to encourage manufacturers to develop devices that work effectively across diverse populations.

Dr. Wilson proposed a simpler approach to assessing disparate performance by directly comparing the mean difference in bias between individuals with dark skin and those with white skin. He suggested setting a threshold for this difference, above which the performance would be considered non-disparate.

Dr. Brown raised questions about labeling and potential actions regarding non-compliant devices already on the market, suggesting the possibility of adding black box warnings or removing them from the market. **Dr. Eydelman** indicated that the agency would consider recommendations and determine the best course of action to maximize public health impact.

Dr. Saville and **Dr. Wilson** discussed the complexity of the proposed model for assessing disparate performance and suggested simplifications. **Dr. Saville** explained that the model compares biases across different skin tones on a continuous scale, rather than dividing them into distinct groups. **Dr. Wilson** emphasized the need for a simpler approach to understanding the differences in bias between skin tones, focusing on mean differences rather than complex models.

Dr. Cassiere initiated a discussion about the acceptable variance in intergroup differences in bias between different skin tones. **Dr. Ballman** emphasized that it's more of a clinical question than a statistical one and sought input from panel members regarding what level of difference would be concerning. **Dr. Saville** pointed out the importance of considering the clinical relevance of differences in bias between skin tones, especially when both groups are within clinically acceptable limits. **Dr. Lanzafame** echoed this sentiment, emphasizing the need to determine at what point differences become clinically relevant for both groups.

Dr. Feldman suggested reframing the question to focus on ensuring that the performance of devices remains clinically acceptable for all patients regardless of skin tone, rather than solely considering the absolute difference between groups.

Dr. Lewis highlighted the importance of maintaining a specific range of oxygen saturation (SAT) levels, especially in neonatology, citing the SUPPORT Trial published in the New England Journal of Medicine in 2010 as evidence. **Dr. Cassiere** referenced a 1990 study by Martin Tobin, emphasizing the difference in oxygen saturation between white and dark-skinned patients and its implications for oxygen delivery. He proposed discussing the idea of establishing a threshold for oxygen saturation levels to ensure patients remain within a safe range, particularly focusing on the 90 percent threshold.

Dr. Wilson contributed to the discussion by mentioning the potential risks associated with both low and high oxygen saturation levels, particularly in neonates, while **Dr. Cassiere** emphasized the need to determine a threshold to ensure patients' oxygen saturation remains within a safe range, citing clearer evidence in the adult population regarding liberal versus conservative oxygenation strategies.

Dr. Feldman highlighted the complexity facing the FDA regarding setting performance standards for pulse oximeters. He noted the diverse needs of different patient populations, such as those in ICUs versus neonatal intensive care units (NICUs), which may require different levels of oxygen saturation monitoring. **Dr. Feldman** raised the question of whether the FDA should establish a universal performance standard that caters to all patient populations or set a minimum standard and allow the market to offer specialized devices for specific clinical settings. He emphasized the importance of determining the target patient populations before providing definitive guidance on performance standards for pulse oximeters.

Dr. Goldman sought clarification on the question regarding pulse oximeter performance standards and labeling. **Dr. Eydelman** explained that the FDA was seeking input on whether additional analysis at specific clinical thresholds should be included in pre-market submissions and how the results of such analysis should be communicated in the labeling. **Dr. Feldman** emphasized the importance of focusing on accuracy range rather than specific thresholds for clinical decision-making. He suggested that while information about diagnostic performance, such as ROC curves, could be valuable, the primary focus should be on accuracy. **Dr. Cassiere** raised the point that clinical therapies often rely on specific thresholds, such as in COVID therapy, prompting discussion on whether these thresholds should be considered in setting pulse oximeter standards.

Dr. Brown, Dr. Wiswell, and **Dr. Gooden** all concured that while requiring additional performance data within the critical range of 87 to 93 for pre-market submissions makes sense, they oppose including detailed thresholds for hypoxemia in the label. They emphasized the importance of considering the context of the patient, their age, and any additional comorbidities when determining oxygenation thresholds.

QUESTION 3

Dr. Lee clarified that "over the counter" doesn't imply general wellness but rather refers to the ability to purchase a medically approved pulse oximeter without a prescription. **Dr. Feldman** expressed his view that there should not be different criteria for evaluating performance based on whether a device is for medical or non-medical use. He suggested labeling devices that do not meet medical standards clearly to indicate they are not suitable for medical purposes, akin to warning labels on cigarette or alcohol products.

Dr. Goldman sought clarification on the nature of over-the-counter (OTC) pulse oximeters, questioning whether they are distinct products from those available for medical use or simply the same devices with different labeling for non-medical consumers. **Dr. Lee** explained that some wearables with medical purposes have OTC indications, and the FDA is considering future scenarios where medical devices become more accessible to consumers. **Dr. Goldman** likened OTC pulse oximeters to non-invasive blood pressure monitors or thermometers commonly available at corner stores, emphasizing the importance of clear instructions and labeling for lay users who may lack medical expertise. **Dr. Goldman** also highlighted the need to consider factors such as device stability and intended use beyond just disparate performance in discussions about pulse oximeters.

Dr. Brown emphasized the importance of maintaining the same high standards for both medical-grade and over-the-counter pulse oximeters. **Ms. Brummert** echoed this sentiment, expressing her reliance on pulse oximeters for making decisions about seeking medical care and advocating for consistent standards across both medical-grade and over-the-counter devices. **Dr. Lanzafame** stressed the need for clear and explicit labeling to ensure that users understand how to use the devices properly.

Dr. Goldman emphasized the importance of ensuring accurate readings, especially for devices used by lay users. **Dr. Gooden** supported the idea of maintaining consistent standards regardless of the context in which the pulse oximeter is used.

Dr. Lee explained that current pulse oximeters available for purchase are often labeled for specific purposes, such as sports and aviation or general wellness. And mentioned the importance of updating labeling and recommendations to align with technological innovations and future sponsor collaborations.

Dr. Cassiere summarized the panel's consensus that there should be a higher standard for over-the-counter medical-grade pulse oximeters. However, concerns were raised about the potential cost implications and whether meeting the same criteria as hospital-grade devices would make them prohibitively expensive.

Dr. Feldman suggested that devices could be marked with a symbol indicating their lack of regulatory approval, akin to the warnings on cigarette packs or alcohol bottles. **Dr. Goldman** echoed concerns about accessibility, noting that language barriers and long lines at pharmacies could hinder consumers' ability to receive guidance. He proposed using QR codes to provide accessible and multilingual instructions and information about device usage, potentially including videos and animations.

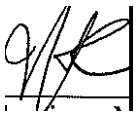
Dr. Lee clarified that patients can order prescription-use pulse oximeters. The discussion then shifted to considerations for patients who obtain over-the-counter pulse oximeters for self-monitoring purposes, without direct physician involvement.

Ms. Brummert inquired about the possibility of FDA reclassifying all pulse oximeters as Class II devices, but the conversation was not extended further due to time constraints.

ADJOURNMENT

Dr. Cassiere concluded the panel meeting by inviting any final summation comments or clarifications from the panel. Since there were no responses, Dr. Cassiere proceeded to thank the panel members, the FDA, the invited speakers, and all participants for their contributions to the meeting.

I approve the minutes of this meeting as recorded in this summary.



Hugh A. Cassiere, M.D., F.C.C.P., F.A.C.P.
Chairperson

I certify that I attended this meeting on February 2, 2024 and that these minutes accurately reflect what transpired.

Candace J. Nalls -S
Digitally signed by Candace J. Nalls -S
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