Accuracy and precision of peripheral capillary oxygen saturation of reprocessed pulse oximetry sensors compared to oxygen saturation in arterial blood samples assessed by CO-oximetry in neonates.

Protocol Number MED-2020-DIV65-001

May 9, 2022
Version 3.0

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INVESTIGATOR ACKNOWLEDGMENT SIGNATURE

- I agree to conduct the study in accordance with the relevant, current protocol and will make changes in the protocol only after notifying the Sponsor, except when necessary to protect the safety, rights, or welfare of subjects.
- I agree to personally conduct and supervise the investigation as described within.
- I agree to inform all subjects that the study products are being used for the purposes of an investigational study.
- I will ensure that requirements relating to obtaining informed consent in the guidelines for Good Clinical Practices (GCP), and 21 Code of Federal Regulation (CFR) Part 50 and Institutional Review Board (IRB) review and approval in 21 CFR Part 56 are met.
- I agree to report to the Sponsor, IRB and/or Ethics Committee, according to the protocol, adverse experiences that occur during the course of the investigation in accordance with guidelines for GCP, and 21 CFR 812.
- I have read and understand the information in the protocol, including the potential risks.
- I agree to maintain adequate and accurate records in accordance with guidelines for GCP and 21 CFR 812.140 and to make those records available for inspection.
- I will ensure that an IRB compliant with the requirements of guidelines for GCP and 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others.
- I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in the guidelines for GCP, and the CFR.

I have received and reviewed this Investigational Plan. I will conduct the study as described.

Principal Investigator (Print):	
Principal Investigator (Signature):	Date (DD-MMM-YYYY)

DOCUMENT HISTORY

VERSION	DATE	DESCRIPTION
Version 1.0	July 30, 2021	Initial draft
Version 2.0	December 9, 2021	Following changes were made: 1. The Medline clinical designee or Medline Director of Clinical Operations name was changed from Kara Cassady to Julie A. Miller. 2. The Medline clinical designee or Medline Director of Clinical Operations phone number was also updated.
Version 3.0	May 9, 2022	Following changes were made: 1. Medline Industries, Inc. was changed to Medline Industries, LP throughout the document. 2. Section 1.1: i) An addition was made in the study population section to indicate that the same blood draw value can be used for multiple sensors placed simultaneously. ii) The description of the site was changed from multiple centers to multiple neonatal intensive care centers in order to be more specific. 3. The study staff was changed to PI or designee throughout the document where applicable. 4. Section 1.2: An addition was made in the required assessments and activities column to indicate that the pulse oximeter data will be collected to determine SpO_2 from same or different hands and/or feet using one or both of the provided sensor types. 5. Section 4.1: Since the data were collected from a convenience sample of subjects, randomization

		will not be required to be completed. An edit was made to indicate that this study is not a randomized clinical trial. 6. The edits were made (where applicable) to indicate that the maximum number of blood draws will be per the standard of care (SOC) of that facility. 7. Section 4.2: An edit was made in the end of the study participation definition with regard to reaching the maximum duration of sensor wear time. It was updated to be per the SOC of the facility or the instructions for use (IFU) of the sensor, whichever occurs first. 8. Section 6.2.1: An edit was made in the collection of arterial blood sample and measurement by CO-oximeter to indicate that the data pairs may be concurrently collected for each of the two sensor types if the sensors can be placed on separate extremities. 9. Section 6.2.6: More clarity was provided regarding removing and/or reusing the sensors. 10. Section 8.1: More clarity was provided for the sample size determination. 11. Section 9.4: The table was updated to include all the abbreviations used in this protocol. 12. Minor changes were made in the protocol including naming conventions, abbreviations, and wording used in our current protocol template.

1. PROTOCOL SUMMARY

1.1. Synopsis

Title:	Accuracy and precision of peripheral capillary oxygen saturation of reprocessed pulse oximetry sensors compared to oxygen saturation in arterial blood samples assessed by CO-oximetry in neonates.
Study Description:	Pulse oximetry helps in measuring peripheral capillary oxygen saturation (SpO_2) continuously and non-invasively, and provides an indirect measurement of arterial oxygenation (SaO_2) based on the red and infrared light-absorption characteristics of oxygenated and deoxygenated hemoglobin. Uses of pulse oximetry include detection of hypoxia, avoidance of hyperoxia, titration of fractional inspired oxygen, and enabling weaning from mechanical ventilation. Arterial blood gas (ABG) analysis, such as by the use of CO-oximeter, provides a direct measurement of SaO_2. However, ABG analysis requires time, expense, and arterial access. Therefore, this study aims to validate the SpO_2 accuracy of pulse oximetry sensors (manufactured by Nellcor and Masimo, and reprocessed by Medline Industries, LP) in neonates as compared to ABG measurements as part of their clinical standard of care (SOC), as assessed by CO-oximetry.
Objective:	To validate the SpO_2 accuracy, bias, and precision of Medline's reprocessed pulse oximetry sensors as compared to SaO_2 in arterial blood samples as assessed by CO-oximetry in neonates.
Endpoint:	Pulse oximeter and co-oximeter reading pair used to determine the accuracy of each pulse oximeter by evaluating accuracy root mean square (A_{RMS}), bias, and precision.

Study Population:	A total of at least 80 total data pairs per sensor will be collected. These should be collected from a minimum of 27 subjects such that there are no more than three pairs per subject (maximum of 3 blood draws). The same blood draw value can be used for multiple sensors placed simultaneously. Inclusion Criteria • Subjects who are postnatal 28 days or younger (neonates) • Subjects who are likely to receive one or more ABG measurements as part of their clinical SOC. • Subjects who weigh less than 5 Kg (weight range for the sensors) Exclusion Criteria • Subjects with current signs and symptoms of a clinically significant Patent Ductus Arteriosus (PDA) combined with a current or planned arterial line placement which will affect the validity of the co-oximetry measurement • Subjects with physical malformation of hands, fingers, feet, or toes that would limit the ability to place sensors for this study • Subjects judged by the Principal Investigator (PI) to be inappropriate for participation in this study • Subjects for whom placing a pulse oximeter will cause dermatological issues (e.g. allergic to foam rubber or adhesive tape)
Phase:	Post-Market
Description of Sites/Facilities Enrolling subjects:	Multiple neonatal intensive care centers
Description of Study:	Data collection will take place at the sites. The PI or designee will place one or both of the pulse oximeter sensors (Medline ReNewal™ Reprocessed Masimo LNCS Series SpO2 Adhesive Sensors, Neo (2329) and Medline Renewal™ Reprocessed Nellcor™ OxiMax SpO2 Sensor, MAXN) on hands and/or feet of the subjects according to the IFU and record the readings. The arterial blood sample used in this study will be taken in the normal course of care and will be measured in the reference CO-oximeter

	for SaO_2. This arterial sample will be obtained from a systemic artery.
Anticipated Enrollment period:	Six months to one year
Subject Duration:	Approximately 15 episodic minutes at the time of the blood draw (the sensor, disconnected from the monitor, may stay on the subject for the maximum allowable duration of sensor use) or per the facility SOC.

1.2 Schedule of activities

REQUIRED ASSESSMENTS & ACTIVITIES	Screening Visit Day 0[a]	Study Visit Day 1[a]
Informed consent and screening form[b]	X	
Arterial blood sample, which is collected in the normal course of care, will be measured in the reference CO-oximeter for SaO_2		X
Pulse oximeter data will be collected to determine SpO_2 from same or different hands and/or feet using one or both of the provided sensor types		X
Adverse event assessment	X----------X	

a: Day 0 and Day 1 visits can be on the same day.
b: Informed consent and screening may be performed on different days.

2. INTRODUCTION

2.1. Background & Rationale

Pulse oximetry helps in measuring SpO_2 continuously and non-invasively, and also provides an indirect measurement of SaO_2 based on the red and infrared light-absorption characteristics of oxygenated and deoxygenated hemoglobin. The ABG analysis, such as by the use of CO-oximeter, provides a direct measurement of SaO_2.[1,2] However, ABG analysis requires time, expense, and arterial puncture; therefore non-invasive techniques that give similar results are being investigated.

This study aims to validate the SpO_2 accuracy and precision of pulse oximetry sensors (manufactured by Nellcor and Masimo, and reprocessed by Medline Industries, LP) in neonates as compared to ABG measurements as part of their clinical SOC, as assessed by CO-oximetry.

2.2. Study Products

2.2.1. Medline ReNewal™ Reprocessed Masimo LNCS Series SpO2 Adhesive Sensors, Neo (2329) (henceforth referred to as "Masimo sensor")

The Masimo sensors are indicated for monitoring SpO_2 and pulse rate for use with neonatal patients in hospitals, hospital-type facilities, mobile, and home environments. Further information on these sensors can be found in Appendix 11.1.1.

2.2.2. Medline Renewal™ Reprocessed Nellcor™ OxiMax SpO2 Sensor, MAXN (henceforth referred to as "Nellcor sensor")

The Nellcor sensors are used for monitoring SpO_2 and pulse rate on neonates. Further information on the products can be found in Appendix 11.1.2.

2.3. Risk/Benefit Profile

2.3.1. Potential Study Risks

Masimo and Nellcor sensors are contraindicated for use on patients who exhibit allergic reactions to foam rubber products and/or adhesive tape. While we are screening to not include subjects with dermatological issues, some subjects with unidentified issues may be enrolled. Subjects will be under the care of a physician who will be able to appropriately address any potential reaction from these products. Although protective measures are taken by the sponsor and site, there is a risk of potential disclosure of Protected Health Information (PHI) by being enrolled in this study.

2.3.2. Potential Study Benefits

There are no direct benefits to the neonates enrolled in this study or to their families. The societal benefit is knowing if the reprocessed sensors are accurate and precise.

2.3.3. Assessment of Potential Risk/Benefit Profile

The use of these products presents minimal risk for subjects enrolled in this study, while offering the potential for societal benefit. Therefore, the risk-benefit profile for the study is favorable.

3. OBJECTIVES AND ENDPOINTS

OBJECTIVE	ENDPOINT	JUSTIFICATION FOR ENDPOINT
To validate the SpO_2 accuracy, bias, and precision of Medline's reprocessed pulse oximetry sensors as compared to SaO_2 in arterial blood samples as assessed by CO-oximetry in neonates.	Pulse oximeter and co-oximeter reading pair used to determine the accuracy of each pulse oximeter by evaluating accuracy root mean square (A_{RMS}), bias, and precision.	CO-oximetry is an invasive technique requiring blood draw(s), whereas pulse oximetry does not involve any blood draw.

4. STUDY DESIGN

4.1. Overall Design

This study is a multi-site, open-label clinical trial validating the SpO_2 accuracy and precision of Medline's reprocessed pulse oximetry sensors as compared to SaO_2 in arterial blood samples as assessed by CO-oximetry in neonates. The data collection will take place at the sites. The PI or designee will place the Masimo and Nellcor sensors on hands and/or feet of the subject according to the IFU and record the reading. The arterial blood sample used in this study will be taken in the normal course of care and will be measured in the reference CO-oximeter for SaO_2. This arterial sample will be obtained from a systemic artery.

4.2. End of Study Definition

A subject's participation in the study may end at several critical points:

- When the maximum number of blood draws, as per SOC (three), has been reached

- The maximum duration of sensor wear time has been reached, as per SOC or IFU, whichever occurs first.
- The PI or patient care team believes it is in the subject's best interest to discontinue in the study.
- Parent or legal guardian of the subject withdraws the subject from the study for any reason.

If the subject withdraws from the study, they will be replaced by another subject.

The study will be considered complete upon issuance of a Clinical Study Report that has been approved by the Clinical Affairs Director.

5. STUDY POPULATION

5.1. Inclusion Criteria

Subjects, who satisfy *ALL* of the inclusion criteria below, will be eligible to participate in the study:

- Subjects who are postnatal 28 days or younger (neonates).
- Subjects who are likely to receive one or more arterial blood gas measurements as part of their clinical standard of care
- Subjects who weigh less than 5 Kg (weight range for the sensors).

5.2. Exclusion Criteria

Subjects, who meet *ANY* of the criteria below, will be ineligible for the study:

- Subjects with current signs and symptoms of a clinically significant PDA, combined with a current or planned arterial line placement which will affect the validity of the co-oximetry measurement.
- Subjects with physical malformation of hands, fingers, feet, or toes that would limit the ability to place sensors for this study.
- Subjects judged by the PI to be inappropriate for participation in this study.
- Subjects for whom placing a pulse oximeter will cause dermatological issues (e.g., allergic to foam rubber or adhesive tape).

5.3. Strategies for Recruitment and Retention

The site PIs and their staff regularly care for neonates and will recruit eligible subjects from their practice. Each site will clearly and adequately convey that participation is voluntary, and that refusal by the parent or legal guardian of the subject will not impact the care and/or medical treatment provided to the subject.

6. STUDY PROCEDURES AND ASSESSMENTS

6.1 Day 0 – Screening Visit and Informed Consent

6.1.1 Informed Consent

Prior to conducting study activities, written consent will be obtained from the parent(s) or legal guardian(s) of all participating subjects and documented on an informed consent form (ICF) that has been approved by an IRB/Ethics Committee. The ICF must be written in adherence to Good Clinical Practice (GCP) and comply with all elements required by FDA CFR 50.25 and ICH 4.8, state and local regulations, and additional elements relevant to specific study situations, (including a statement that Medline Industries, LP and authorities have access to subject records). A copy of the ICF will be given to the parent(s) or legal guardian(s) of the subject.

6.1.2 Eligibility Screening

Potential subjects will be screened for eligibility by the site PI, via a combination of the screening form provided by Medline Industries, LP, and by a review of the potential subject's medical chart by the site PI and/or their staff.

6.2. Day 1 – Study visit

6.2.1. Collection of arterial blood sample and measurement by CO-oximeter

The arterial blood sample will be collected in the normal course of care and will be measured in the reference CO-oximeter for SaO_2. The time of the arterial blood sample will be recorded on the CRF by the PI or designee or patient's care team using a calibrated clock as the reference time. No more than three blood draws, resulting in three data pairs per sensor in a subject, will be used for this study. Data pairs may be concurrently collected for each of the two sensors type if sensors can be placed on separate extremities.

6.2.2. Data collection using pulse oximeter

At or near the time the first blood sample is collected, the PI or designee will place one or both sensors (Masimo and/or Nellcor sensors) on the subject. If the subject is currently receiving biliruben light therapy, then the biliruben light must be turned off when the pulse oximeter sensor reading is taken. The PI or designee will record the SpO_2 measurement, the subject's heart rate, and the time and location of the measurement on the CRF using a calibrated clock as the reference time.

6.2.3 Timing of Data Collection

The ideal time to collect SpO_2 values is <1 minute of the arterial blood sample collection. However, the PI or designee may collect the SpO_2 values up-to 10 minutes before or 10

minutes after the arterial blood sample is collected. It is also ideal to collect both SpO_2 values at the same time. If this is not possible, it is acceptable to collect the SpO_2 values at different times, but still within the ±10-minute timeframe of when the arterial blood sample was collected.

6.2.4 Placement of Study Pulse Oximeters

The ideal placement of the sensors is to be on the same location (e.g., same foot, hand, finger, or toe). If this placement is not possible, it is permissible to place the sensors onto different locations.

6.2.5 Conflicting Choice of Same Location versus Same Time

If the preference of measurements at the same time and at the same location cannot both be accommodated, the PI or designeewill be advised to use personal judgement and preferentially pick the solution that will give the most similar measurement (that is selecting the same location (if the patient has a stable SpO_2 over time), or selecting the same time (if the patient has markedly different SpO_2 or perfusion suspected between measurement locations)).

6.2.6 Moving and Removing Sensors

The sensors may remain on the subject up-to the same duration as would be used for a SOC pulse oximeter. Thus, the duration the sensors remains on the subject is variable but limited by the SOC for each subject.

Subject specific sensors that are removed in between samplings will be secured by the study team until the next time point use. Sensors may be reused on the same subject but will not be used on another subject. Once a subject has completed participation, their sensor will be collected and returned to Medline Industries, LP.

The study or clinical team may move a sensor from location to location on the subject's body to facilitate care and measurement quality.

If the subject has multiple arterial blood samples collected, 6.2.1-6.2.6 can be repeated up to three times using the same sensor. If a new sensor is used, it shall be noted in the CRF.

6.2.7 Additional Data Collected

Additional data recorded on the CRF will include the subject’s gestational age, days of life, weight, length, reason for admission, and skin tone. The skin tone will be evaluated using the Munsell System Soil Color Chart, Hue 7.5YR. The value score that best matched the subject’s skin on the dorsal surface of the distal extremities was recorded.

7 ADVERSE DEVICE EVENTS

7.1 Definition of Adverse Device Event (ADE)

The ADE is the adverse event (AE) related to the use of an investigational medical device resulting from insufficiencies or inadequacies in the IFU, the deployment, installation, the operation, or any malfunction of the investigational medical device or from error use.

7.2 Definition of Serious Adverse Device Event (SADE)

The SADE is the adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event (SAE).

The FDA definition of SAE will be used in this study: An AE or suspected adverse reaction is considered "serious" if, in the view of either the PI or sponsor, it results in any of the following outcomes:

- Death
- A life-threatening adverse event
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions or,
- A congenital anomaly/birth defect.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the subject's participation and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. All SADEs will be reported to Medline, regardless of potential relationship to the investigational device. SADEs will be reported to the reviewing IRB as necessary according to their rules.

7.3 Definition of Unanticipated Adverse Device Effect (UADE)

Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

7.4 Severity of Adverse Device Event

- **Mild (1 = Grade 1):** Awareness of signs or symptoms, but easily tolerated; are of minor irritant type, causing no loss of time from normal activities; symptoms would not require medication or a medical evaluation; signs and symptoms are transient.

- **Moderate (2 = Grade 2):** Discomfort severe enough to cause interference with usual activities; requiring treatment but not extended hospitalization or intensive care for the subject.
- **Severe (3 = Grade 3):** Incapacitating with inability to do work or usual activities; signs and symptoms may be systemic in nature or require medical evaluation and/or treatment; requiring additional hospitalization or intensive care (prolonged hospitalization).
- **Life-threatening (4 = Grade 4**): At immediate risk of death in view of the investigator, or it is suspected that the use or continued use of the product would result in subject's death; urgent intervention indicated.
- **Death (5 = Grade 5):** Death related to adverse event.

7.5 Relatedness of ADE and SADE

- **Unrelated:** This category applies to those adverse events which, after careful consideration, are clearly and incontrovertibly due to extraneous causes (disease, environment, etc.)
- **Possible:** This category applies to those adverse events for which, after careful medical consideration at the time they are evaluated, a connection with the Investigational Product administration appears unlikely but cannot be ruled out with certainty.
- **Probable:** This category applies to those adverse events which, after careful medical consideration at the time they are evaluated, are felt with a high degree of certainty to be related to the Investigational Product.
- **Definite:** This category applies to those adverse events which, after careful consideration, are clearly and incontrovertibly due to the Investigational Product.

7.6 Expectedness

The site PI will be responsible for determining whether an ADE or SADE is expected or unexpected. An ADE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the medical device.

Expected ADEs include a reaction or irritation at the study site following application of the sensors or the site from where blood is drawn.

7.7 Adverse Device Event Reporting

The ADEs will be recorded on the Adverse Event form, provided by Medline Industries, LP, by the site PI. Changes in the severity of an ADE will be documented to allow an assessment of the duration of the event at each level of severity. Changes in severity will necessitate a new CRF to document the new level of severity. ADEs characterized as intermittent require documentation of onset and duration of each episode.

Non-serious ADEs are to be reported to the study sponsor for review and reported to the IRB per IRB reporting requirements.

7.8 Serious Adverse Device Event and Unanticipated Adverse Device Effect Reporting

The site PI shall complete a SAE Form provided by Medline Industries, LP and submit to the study sponsor, but in no event later than 48 hours after the investigator first learns of the effect. The site PI shall report the SADE to the reviewing IRB, if applicable, according to their reporting requirements. The study sponsor is responsible for conducting an evaluation of the SADE and shall report the results of such evaluation to the FDA and to all reviewing IRBs if applicable within 10 working days after the sponsor first receives notice of the effect. Thereafter, the sponsor shall submit such additional reports concerning the effect as FDA requests.

For questions regarding this process or the event, you may contact your Medline clinical designee or the Medline Director of Clinical Operations:

Name: Julie A. Miller RN, BSN, CCRA
Phone: 630-418-6891
E-mail: clinicaloperations@medline.com

8 STATISTICAL CONSIDERATIONS

8.1 Sample Size Determination

Data from a study assessing the accuracy of both pulse oximeters on an adult population (Study ID # 2018-268) were used as parameters for sample size estimation for this protocol. Sample size estimation was conducted separately for each product using both the Confidence Intervals for One Standard Deviation Using Standard Deviation (as an estimate for the accuracy root mean square A_{RMS} statistic in equation 1.1 below) and Bland-Altman procedures in PASS 2020 Power Analysis and Sample Size Software (2020). NCSS, LLC. Kaysville, Utah, USA, ncss.com/software/pass. The most conservative estimate between the two products for the A_{RMS} sample size (18) and the Bland-Altman statistic (40) was used as the minimum number of data pairs, n. A data pair will consist of a pulse oximeter sensor reading paired with an ABG reading collected by a CO-oximeter. We selected a sample size of at least 80 total data pairs for each of the two product sensors, consisting of at least 40 data pairs per site per product sensor. We doubled this estimate and selected a sample size of at least 80 total data pairs per product sensor, such that no subject contributes more than three data pairs for each of the two product sensors, for a minimum of 27 subjects. The same blood gas value can be used for multiple sensors applied simultaneously.

8.2 Randomization

Randomization will not be completed as the data are collected from a convenience sample of subjects.

8.3. Populations for Analysis

All data pairs will be included for analysis, unless at the time of data acquisition any one or more of the following is true: (1) the SpO2 value is >100%; OR (2) the SpO2 value is ≤0%; OR (3) the heart rate measurement derived from the pulse oximeter is 0 beats per minute; OR (4) the research personnel collecting the data notes an anomaly in the measurement on the CRF at the time of data collection before data analysis begins. Any such designated outliers and/or anomalous data will be explained and any data that is excluded from the analysis will be justified in the final report.

8.4 Data Analysis

Accuracy of each pulse oximeter will be assessed per ISO 80601-2-61:2017, the FDA "Pulse Oximeters - Premarket Notification Submissions [510(k)s] Guidance for Industry and Food and Drug Administration Staff" document issued on March 4, 2013, and paper by Bland et al., 2007.[3,4,5]

For each pulse oximeter, an accuracy root mean square ($\boldsymbol{A_{RMS}}$, in equation 1.1 below) will be calculated to define the SpO_2 accuracy compared to the SaO_2 as measured by co-oximeter, as outlined in ISO 80601-2-61:2017 sub clause 201.12.1.101. It is expected that each of the sensors should achieve an $\boldsymbol{A_{RMS} \leq 3\%}$ as per the testing of these same products in the protocol on adult subjects. In addition, mean Bias ($\boldsymbol{B}$, in equation 1.2) defined per ISO 80601-2-61:2017 as the mean difference between the test and reference values, preserving sign, and precision ($\boldsymbol{SD_{res}}$, in equation 1.3), defined per ISO 80601-2-61:2017 as the standard deviation of the residuals.

In the following equations, let

- SpO_{2_i} be the oxygen saturation value for the i^{th} data pair in the range of interest measured using the pulse oximeter
- SaO_{2_i} be the reference oxygen saturation value for the i^{th} data pair in the range of interest measured using the co-oximeter
- and n be the number of data pairs in the sample in the range of interest.

Then, per ISO 80601-2-61:2017 A_{RMS} is defined as:

$$A_{RMS} = \sqrt{\frac{\sum_{i=1}^{n}\left(SpO_{2_i} - SaO_{2_i}\right)^2}{n}} \tag{1.1}$$

Mean bias B is defined as:

$$B = \frac{\sum_{i=1}^{n}\left(SpO_{2_i} - SaO_{2_i}\right)}{n} \tag{1.2}$$

And precision (SD_{res}) is defined as:

$$SD_{res} = \sqrt{\frac{\sum_{i=1}^{n}\left(SpO_{2_i} - SpO_{2fit_i}\right)^2}{n-2}} \tag{1.3}$$

where SpO_{2fit_i} is the difference between the i^{th} datum and the value of the fitted curve corresponding to the i^{th} reference value

For each pulse oximeter, a Bland-Altman plot (mean vs. difference of SaO_2 and SpO_2) and an error plot (SaO_2 vs. difference of SaO_2 and SpO_2) will be generated. Between and within subject variance and upper and lower 95% limits of agreement will be presented. Subject demographic data will be presented with summary statistics and site-level effects will be assessed as appropriate. Outliers will be explained and any data that is excluded from the data analysis or any deviations from this statistical analysis plan will be justified in the final report.

9 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

9.1 Clinical Monitoring

The Clinical Research Associate (CRA) will confirm that the rights and well-being of subjects are protected, and that the reported trial data are accurate, complete, and verifiable from source documents. Moreover, the CRA will confirm the conduct of the trial by the PI, PI or designee, and sites are in compliance with the protocol, GCP, and regulatory requirements as well as any applicable institution or IRB and federal or local processes. Monitoring will occur every two months, depending on the enrollment during the study duration. It will occur more frequently if:

- The volume or quantity of data is large or there is a backlog of review due to unexpected issues
- This would also include any large volume of CRFs to be reviewed
- The site compliance with the protocol or compliance with expected ICH/GCP and regulatory requirements is lacking or there are continuing unresolved compliance issues
- There are unexpected AE/SAE or subject safety concerns noted
- There are any unexpected inconsistencies with study product management
- There is a request for more frequent monitoring by the site
- Any mutually agreeable situation as determined by the sites and Medline

The frequency of routine monitoring may be increased to a longer interval based off of enrollment. CRA will discuss this with Medline Director or Clinical Manager and will inform the PI prior to implementation.

Monitoring activities will include subject eligibility, source data review, CRF completion verification, product accountability, site continued suitability, PI study oversight, compliance, and all general monitoring activities as outlined in FDAs Code of Federal Regulations and ICH/GCP guidelines that guide that activity.

Medline Industries LP may, on occasion, contract with external Clinical Research Organizations to provide CRA services and those CRAs are authorized to act on behalf of Medline Industries, LP.

It is expected that the site will be compliant with any institutional Standard Operating Procedures during the execution of the protocol and evidence of that compliance should be readily documented and verifiable by the CRA.

The CRA will generate an internal Medline Industries, LP visit report that will be filed with the Medline Industries, LP trial master file and will provide the PI a detailed follow-up letter after each monitoring visit that will outline the completed monitoring activities as well as any identified areas of concern and the expected/applicable corrections needed. Medline Industries, LP reserves the right to perform audit of the study activities – either routine or for-cause – as needed, and may also perform clinical monitoring audit as well.

9.2 Regulatory and Ethical Considerations

9.2.1 Confidentiality and Privacy

Subject confidentiality and privacy is strictly held in trust by the investigators, their staff, and the Sponsor. Therefore, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the Sponsor. All study data and study records will be managed and stored in accordance with the site's HIPAA compliant policies on data storage and security. All electronic transmission of data will adhere to HIPAA Security Rules.

The study monitor, other authorized representatives of the Sponsor, representatives of the IRB and regulatory agencies may inspect all documents and records required to be maintained by the investigators, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the subjects in this study. The clinical study sites will permit access to such records.

A master list linking subject numbers to subject name and medical record number will be maintained in a secure database (paper or electronic) by the site PI. The study subject's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for at least a period of two years, or longer if dictated by the reviewing IRB, Institutional policies, Sponsor requirements, or ICH/GCP and FDA requirements. The PI will agree to notify Sponsor of any intent to move or destroy these documents.

Study subject's research data, which is for purposes of statistical analysis and scientific reporting, will be maintained at the research sites on the CRFs. Copies of the CRFs, which will not contain any identifiable information, will be provided to the Sponsor for the purposes of data analysis. The study data entry and study management systems used by clinical sites and by Medline Industries, LP research staff will be secured and stored in an access controlled locked area (any paper forms) and password protected (electronic

records). At the end of the study, all study databases that are not already de-identified will be de-identified and archived at Medline Industries, LP.

9.2.2 Safety Oversight

The design of this study is such that the ethical issues/special protections, related to children (neonates) as study subjects, have been considered.[6] In addition, given that this is a post-market study on the sensors used in accordance with their IFU and the ISO standard, there is minimal safety risk to participating subjects.[3] The subjects are in care of the site PI who are qualified to provide adequate safety oversight for the study. In the event there any AEs or SAEs, the site PI will review them and make any necessary safety determinations as needed.

9.2.3 Data Handling and Record Keeping

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the PI. The PI is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents of any kind (electronic, paper, etc.) should be completed in accordance with Good Documentation Practices (GDP) to ensure accurate interpretation of data. CRFs will be created for each subject. The CRA will verify the data entered into the CRF with the site source regardless of the type of source. The site will be responsible for developing a written process that ensures the CRA is able view the source data.

Data from the CRFs will be entered by Medline into an electronic spreadsheet via dual-entry to assure no errors. Data will be transferred to and analyzed with Statistical Analysis System (SAS), SAS® 9.4, for statistical analysis. SAS® allows for internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Medline Industries, Inc. will be responsible for performing final data analysis and confirmation of results.

9.2.4 Study Records Retention

Study documents should be retained until at least two years have elapsed since the formal discontinuation of the study intervention or as required by any applicable FDA guidelines or for a longer period if required by local regulations. No records will be destroyed without the written consent of the Sponsor, if applicable. It is the responsibility of the Sponsor to inform the PI when these documents no longer need to be retained. The PI is required to notify Medline if the location of the stored documents is changed after it is defined at the time of the Close Out Visit at study end.

9.2.5 Study Discontinuation

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to the PI, Sponsor, and IRB. If the study is prematurely terminated or suspended, the PI will promptly inform the IRB and Sponsor and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participating subjects as determined by AE review
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the Sponsor and/or IRB.

9.2.6 Study Closeout

Upon completion of the study, Medline and/or its designees will notify the sites of closeout related procedures and will coordinate with the site the return of equipment and/or any unused product. Medline CRA will communicate closely with the PI and co-investigators at that time point and will review all close out steps and materials. All study data, related study documents, and unused study product, will be returned to the Sponsor. Sponsor will provide the facility with a summary of the activities and findings after the final analysis of the data has been completed. The site will also notify the IRB that the study has completed.

9.2.7 Conflict of Interest Policy

The independence of this study from any actual or perceived influence is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication or any aspect of this trial will be disclosed and managed.

9.3 Protocol Deviations

It is the responsibility of the PI or designee to use continuous vigilance to identify and report deviations on a routine basis. All deviations must be addressed in study source documents, and reported to Medline Industries, Inc. Protocol deviations must be sent to the reviewing IRB per their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements.

9.4 Abbreviations

ABG	Arterial Blood Gas
ADE	Adverse Device Event

AE	Adverse Event
CFR	Code of Federal Regulations
CRA	Clinical Research Associate
CRF	Case Report Form
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GDP	Good Documentation Practice
HEOR	Health Economics and Outcomes Research
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IFU	Instructions for Use
IRB	Institutional Review Board
ISO	International Organization for Standards
PDA	Patent Ductus Arteriosus
PHI	Protected Health Information
PI	Principal Investigator
SADE	Serious Adverse Device Event
SAE	Serious Adverse Event
SaO_2	Arterial Oxygenation
SOC	Standard of Care
SpO_2	Peripheral Capillary Oxygen Saturation
UADE	Unanticipated Adverse Device Event

10 REFERENCES

1. Ascha M, Bhattacharyya A, Ramos JA, Tonelli AR. Pulse Oximetry and Arterial Oxygen Saturation during Cardiopulmonary Exercise Testing. Med Sci Sports Exerc. 2018 Oct; 50(10):1992-1997.

2. Dawson JA, Davis PG, O'Donnell CP, Kamlin CO, Morley CJ. Pulse oximetry for monitoring infants in the delivery room: a review. Arch Dis Child Fetal Neonatal Ed. 2007 Jan; 92(1):F4-7.

3. International standard ISO 80601-2-61, Second edition 2017-12. Medical electrical equipment – Part 2-61: Particular requirements for basic safety and essential performance of pulse oximeter equipment. https://www.iso.org/standard/67963.html

4. Pulse Oximeters – Premarket Notification Submissions [510(k)s] Guidance for Industry and Food and Drug Administration Staff. March 4, 2013. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pulse-oximeters-premarket-notification-submissions-510ks-guidance-industry-and-food-and-drug

5. Bland JM, Altman DG. Agreement between methods of measurement with multiple observations per individual. J Biopharm Stat. 2007; 17(4):571-82. doi: 10.1080/10543400701329422. PMID: 17613642.

6. U.S. Department of Health and Human Services. Office of Human Research Protections. https://www.hhs.gov/ohrp/regulations-and-policy/guidance/special-protections-for-children/index.html

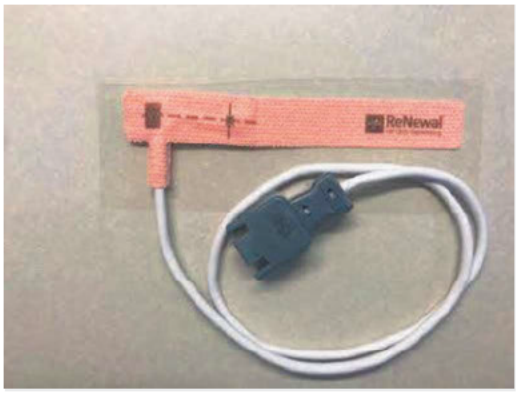
11. APPENDIX

11.1 Study Products

11.1.1 Medline ReNewal™ Reprocessed Masimo LNCS Series SpO2 Adhesive Sensors, Neo (2329)

This Masimo sensor is indicated for monitoring SpO_2 and pulse rate for use with neonatal patients during no-motion conditions, and for patients who are well perfused in hospitals, hospital-type facilities, mobile, and home environments. This sensor is manufactured by Masimo and reprocessed by Medline Industries, Inc. The preferred site for use of this sensor is the foot, but across the palm and back of the hand can also be used. Sensor placement will be chosen at the discretion of the PI.

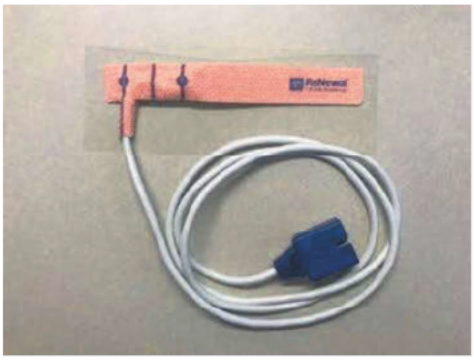
Figure 11.1.1: Medline ReNewal™ Reprocessed Masimo LNCS Series SpO2 Adhesive Sensors, Neo (2329)



11.1.2. Medline Renewal™ Reprocessed Nellcor™ OxiMax SpO2 Sensor, MAXN

This Nellcor sensor is used for monitoring SpO_2 and pulse rate on neonates. It is manufactured by Nellcor and reprocessed by Medline Industries, Inc. The preferred site is the foot but hand can be used too. Sensor placement will be chosen at the discretion of the PI.

Figure 11.1.2: Medline Renewal™ Reprocessed Nellcor™ OxiMax SpO2 Sensor, MAXN



The instructions for use of Masimo and Nellcor sensors can be found in the subsequent pages of this protocol.

Medline ReNewal Reprocessed Masimo LNCS Series Adult, Pediatric, Infant, and Neonatal SpO_2 Adhesive Sensors Models Adtx/Adtx-3, Pdtx/Pdtx-3, Inf-L/Inf-3/Inf, and Neo-L/Neo-3/Neo

Instructions for Use

Read the* Instructions for Use *in their entirety* before *using Medline ReNewal Reprocessed Masimo SpO_2 Adhesive Sensors.

Failure to comply may result in patient and/or healthcare-staff injury.

Description:	Reprocessed device for single use. Reprocessed by Medline ReNewal.
Non Sterile:	The device is supplied non sterile.
Caution:	Federal (USA) law restricts this device to sale by or on the order of a physician.
Contact:	For more information, please call Medline ReNewal Customer Service: 1-866-866-7477.

Description: Medline ReNewal Reprocessed Masimo LNCS Series Adult Pediatric, Infant and Neonatal SpO2 Adhesive Sensors models Adtx/Adtx-3, Pdtx/Pdtx-3, Inf-L/Inf-3/Inf, and Neo-L/Neo-3/Neo. Following clinical use, each sensor is returned to Medline ReNewal where it is cleaned, disinfected, and packaged for an additional clinical use. Each sensor is tracked through the reprocessing cycle to monitor the number of times the sensor has been reprocessed. If sensors are to be used again, they must be returned to Medline ReNewal for reprocessing. Please see Medline ReNewal instructions to healthcare facilities before returning.

The sensor site must be inspected at least every eight hours; and if the circulatory condition or skin integrity has changed, the sensor should be applied to a different site.

INDICATIONS

The Medline ReNewal Reprocessed Masimo LNCS Adult, Pediatric, Infant, and Neonatal adhesive sensors are indicated for single patient use for continuous noninvasive monitoring of functional oxygen saturation of arterial hemoglobin (SpO_2) and pulse rate (measured by an SpO_2 sensor) for use with adult, pediatric, infant, and neonatal patients during no motion conditions, and for patients who are well perfused in hospitals, hospital-type facilities, mobile, and home environments (see Table 1).

Table 1: Medline ReNewal Reprocessed Masimo LNCS SpO_2 adhesive sensors.

Sensor	Adtx Adtx-3	Pdtx Pdtx-3	Inf, Inf-L, Inf-3	Neo, Neo-L, Neo-3
Body weight	> 30 kg	10 - 50 kg	3 - 20 kg	< 5 kg > 40 kg
Application site	Finger or toe	Finger or toe	Thumb or great toe	Neonatal: hand or foot Adult: finger or toe

CONTRAINDICATIONS

The Medline ReNewal Reprocessed LNCS sensors are contraindicated for patients who exhibit allergic reactions to foam rubber products and/or adhesive tape.

WARNINGS

- Do not use if package is damaged.
- All sensors and cables are designed for use with specific monitors. Verify the compatibility of the monitor, cable and sensor before use, otherwise degraded performance and/or patient injury can result.
- The site must be checked frequently or per clinical protocol to ensure adequate adhesion, circulation, skin integrity and correct optical alignment.
- Circulation distal to the sensor site should be checked routinely.
- Do not use tape to secure the sensor to the site; this can restrict blood flow and cause inaccurate readings. Use of additional tape can cause skin damage, and/or pressure necrosis or damage the sensor.
- Sensors applied too tightly or that become tight due to edema will cause inaccurate readings and can cause pressure necrosis.
- Misapplied sensors or sensors that become partially dislodged may cause incorrect measurements.
- Venous congestion may cause under reading of actual arterial oxygen saturation. Therefore, assure proper venous outflow from monitored site. Sensor should not be below heart level (e.g. sensor on hand of a patient in a bed with arm dangling to the floor).
- Venous pulsations may cause erroneous low SpO_2 readings (e.g. tricuspid value regurgitation).
- The pulsations from intra-aortic balloon support can be additive to the pulse rate on the oximeter pulse rate display. Verify patient's pulse rate against the ECG heart rate.
- The sensor should be free of visible defects, discoloration and damage. If the sensor is discolored or damaged, discontinue use. Never use a damaged sensor or one with exposed electrical circuitry.
- Carefully route cable and patient cable to reduce the possibility of patient entanglement or strangulation.
- Avoid placing the sensor on any extremity with an arterial catheter or blood pressure cuff.

- If using pulse oximetry during full body irradiation, keep the sensor out of the radiation field. If sensor is exposed to the radiation, the reading might be inaccurate or the unit might read zero for the duration of the active radiation period.
- Do not use the sensor during MRI scanning or in a MRI environment.
- High ambient light sources such as surgical lights (especially those with a xenon light source), bilirubin lamps, fluorescent lights, infrared heating lamps, and direct sunlight can interfere with the performance of the sensor.
- To prevent interference from ambient light, ensure that the sensor is properly applied, and cover the sensor site with opaque material, if required. Failure to take this precaution in high ambient light conditions may result in inaccurate measurements.
- High levels of COHb or MetHb may occur with a seemingly normal SpO_2. When elevated levels of COHb or MetHb are suspected, laboratory analysis (CO-Oximetry) of a blood sample should be performed.
- Elevated levels of Carboxyhemoglobin (COHb) may lead to inaccurate SpO_2 measurements.
- Elevated levels of Methemoglobin (MetHb) will lead to inaccurate SpO_2 measurements.
- Elevated Total Bilirubin levels may lead to inaccurate SpO2 measurements.
- Intravascular dyes such as indocyanine green or methylene blue or externally applied coloring and texture such as nail polish, acrylic nails, glitter, etc. may lead to inaccurate SpO_2 measurements.
- Inaccurate SpO_2 readings may be caused by severe anemia, low arterial perfusion or motion artifact.
- To prevent damage, do not soak or immerse the sensor in any liquid solution.
- Do not modify or alter the sensor in any way. Alteration or modification may affect performance and/or accuracy.
- Do not attempt to reuse on multiple patients, reprocess, recondition or recycle sensors or Masimo patient cables as these processes may damage the electrical components, potentially leading to patient harm.
- High oxygen concentrations may predispose a premature infant to retinopathy. Therefore, the upper alarm limit for the oxygen saturation must be carefully selected in accordance with accepted clinical standards.
- **Caution**: Replace the sensor when a replace sensor message is displayed, or when a low SIQ message is consistently displayed after completing the low SIQ troubleshooting steps identified in the monitoring device operator's manual.
- **Note**: The sensor is provided with X-Cal™ technology to minimize the risk of inaccurate readings and unanticipated loss of patient monitoring. The sensor will provide up to 168 hours of patient monitoring time. After single-patient use, discard sensor.

Instructions: Sensor and Cable

A. Site Selection

- Always choose a site that is well perfused and will completely cover the sensor's detector window.
- Site should be cleaned of debris and dry prior to sensor placement.

LNCS Adtx and Adtx-3 Adult Sensors

- 30 kg: The preferred site is the middle or ring finger of non-dominant hand.

LNCS Pdtx and Pdtx-3 Pediatric Sensors

- 10 - 50 kg: The preferred site is middle or ring finger of non-dominant hand.

LNCS Inf, Inf-L and Inf-3 Infant Sensors

- 3 - 20 kg: The preferred site is the great toe. Alternatively, the toe next to the great toe or the thumb can be used.

LNCS Neo, Neo-L and Neo-3 Neonatal/Adult Sensors

- < 5 kg: The preferred site is the foot. Alternatively, across the palm and back of the hand can be used.
- > 40 kg: The preferred site is the middle or ring finger of non-dominant hand.

B. Attaching the Sensor to the Patient

1. Open the pouch and remove the sensor. Remove the backing from the sensor, if present.

Adult (> 30 kg) and Pediatric (10 - 50 kg)

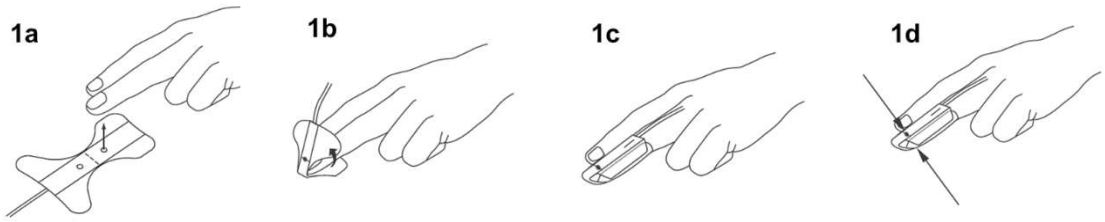


Figure 1: Adtx 1859, Adtx-3 2317, Pdtx 1860, and Pdtx 2318

2. Refer to **Fig. 1a**: Orient the sensor cable so that the detector can be placed first. Place the tip of the finger on the dashed line with the fleshy part of the finger covering the detector window.
3. Refer to **Fig. 1b**: Press the adhesive wings one at a time onto the finger. Complete coverage of the detector window is needed to ensure accurate data.
4. Refer to **Fig. 1c**: Fold the sensor over the finger with the emitter window (star) positioned over the fingernail. Secure the wings down one at a time around the finger.

5. Refer to **Fig. 1d**: When properly applied, the emitter and detector should be vertically aligned.
6. Verify correct positioning and reposition if necessary (the black lines should align).

Infants (3 - 20 kg)

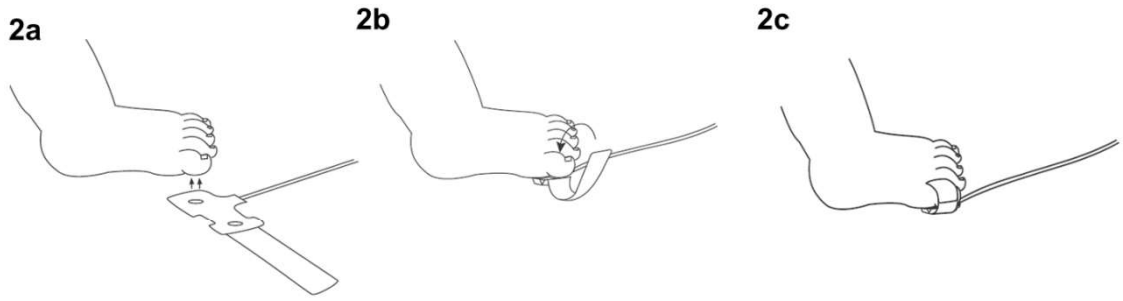


Figure 2: Inf 2328, Inf-L 1861, and Inf-3 2319

7. Refer to **Fig. 2a**: Direct the sensor cable so that it either points away from the patient or runs along the bottom of the foot. Position the detector onto the fleshy part of the great toe. Complete coverage of the detector window is needed to ensure accurate data.
8. Refer to **Fig. 2b**: Wrap the adhesive wrap around the toe and ensure that the emitter window (star) aligns on the top of the toe directly opposite the detector.
9. Refer to **Fig. 2c**: Verify correct positioning and reposition if necessary.

Neonates (< 5 kg)

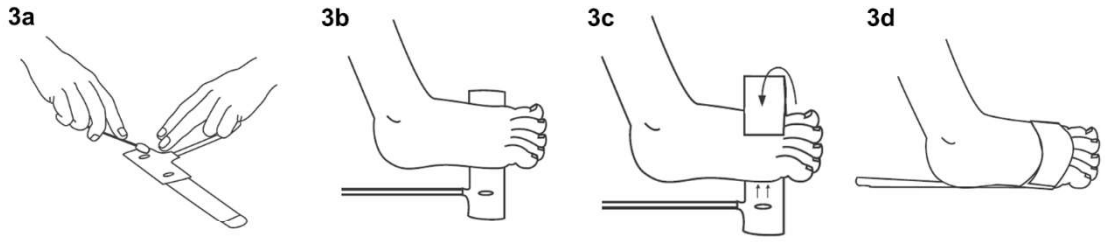


Figure 3: Neo 2329, Neo-L 1862, and Neo-3 2320

10. Refer to **Fig. 3a**: For fragile skin, the stickiness of the medical grade adhesive can be diminished or eliminated by daubing the adhesive areas with a cotton ball or with gauze.
11. Refer to **Fig. 3b**: Direct the sensor cable so that it either points away from the patient or runs along the bottom of the foot. Apply the detector onto the fleshy part of the lateral aspect of the sole of the foot aligned with the fourth toe. Alternatively,

the detector may be applied to the top of the foot (not shown). Complete coverage of the detector window is needed to ensure accurate data.

12. Refer to **Fig. 3c**: Wrap the adhesive/foam wrap around the foot and ensure that the emitter window (star) aligns directly opposite of the detector. Be careful to maintain proper alignment of the detector and emitter windows while attaching adhesive/foam wrap to secure the sensor.
13. Refer to **Fig. 3d**: Verify correct positioning and reposition if necessary.

C. Attaching the Sensor to the Patient Cable

Refer to **Fig. 4:** Insert the connector completely into the patient cable connector (1). Completely close the protective cover (2).

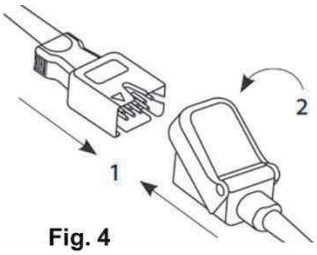


Fig. 4

D. Disconnecting the Sensor from the Patient Cable

Refer to **Fig. 5**. Lift the protective cover to gain access to the sensor connector (1). Pull firmly on the sensor connector to remove from the patient cable (2).

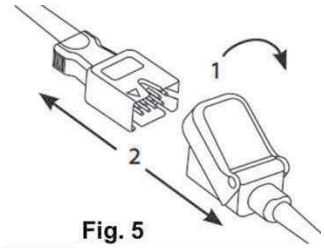


Fig. 5

CAUTION

To prevent damage, do not soak or immerse the sensor in any liquid solution.

ACCURACY SPECIFICATIONS

The Medline ReNewal Reprocessed Masimo LNCS SpO_2 sensors are indicated for the following conditions:

- SpO_2 range: 70 – 100%
- Pulse rate: 25 – 240 bpm
- Operating temperature: 5 – 40ºC
- Storage temperature: -40 – 70ºC
- Humidity: 5 – 95%

Table 2 provides the specifications of Medline ReNewal Reprocessed Masimo LNCS SpO_2 Sensors.

Table 2: Medline ReNewal Reprocessed Masimo LNCS SpO_2 sensors' specifications.

Model Number	Sensor Type	Application Site	Saturation Accuracy	Pulse Rate Accuracy	Patient Weight (kg)
Adtx 1859, Adtx-3 2317	Adult Adhesive Sensor	Finger	± 2%	± 3 bpm	> 30
Pdtx 1860, Pdtx-3 2318	Pediatric Adhesive Sensor	Finger	± 2%	± 3 bpm	10 – 50
Inf 2328, Inf-L 1861, Inf-3 2319	Infant Adhesive Sensor	Toe	± 2%	± 3 bpm	3 – 20
Neo 2329, Neo-L 1862, Neo-3 2320	Neonatal/Adult Adhesive Sensor	Foot/Finger	± 2% in adults	± 3 bpm	< 5 kg > 40 kg

Table 3 shows the root mean square of the error (A_{RMS}) values measured using the Medline ReNewal Reprocessed Masimo LNCS SpO_2 Sensors, models Adtx 1859 and Neo 2329, in a clinical study on adult volunteers. A grouping strategy was used for testing and therefore two representative sensor models were utilized to obtain data. The data obtained by the sensor model Adtx represents the accuracy specifications of the Adtx-3, Pdtx, and Pdtx-3 devices and the data obtained for the sensor model Neo represents the accuracy specifications of the Neo-L, Neo-3, Inf, Inf-L, and Inf-3 devices.

All specifications were validated with the Masimo Radical 7 with Rainbow technology Pulse Oximeter system.

Table 3: Summary of accuracy data collected during the adult clinical validation study.

Model Under Test	Saturation Range (%)			
	70 – 100	90 – 100	80 – 90	70 – 80
Adtx 1859 A_{rms}[a]	1.8	1.1	1.8	2.2
Neo 2329 A_{rms}	1.6	0.9	1.6	2.1
[a] A_{rms} = average root mean square.				

Figures 6 and 7 provide graphical representation of sample data points acquired during the adult clinical trial using the Medline ReNewal Reprocessed Masimo LNCS SpO_2 Sensors.

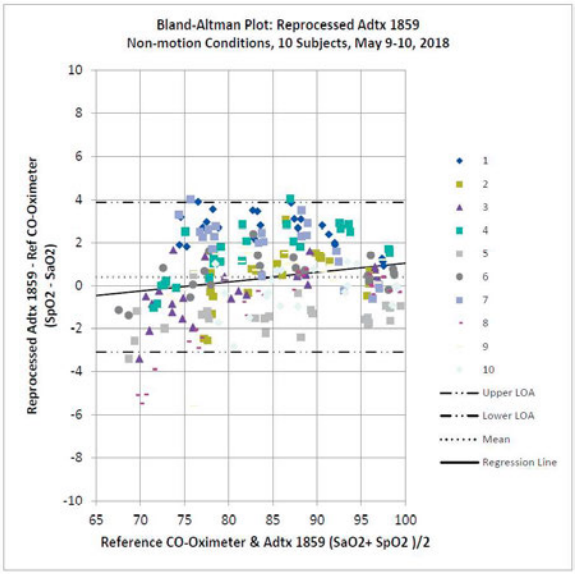


Fig. 6: **Bland-Altman plot of all sampled data points by subject for the adult clinical study for the Medline ReNewal Reprocessed Masimo Adtx 1859 sensor with linear regression fit and upper and lower 95% limits of agreement.**

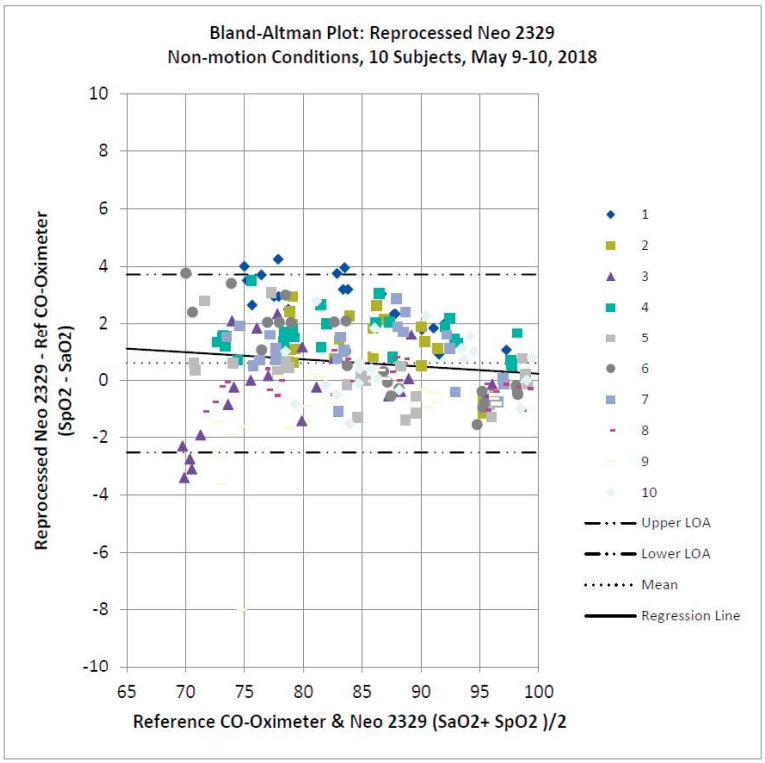


Fig.7: **Bland-Altman plot of all sampled data points by subject for the adult clinical study for the Medline ReNewal Reprocessed Masimo Neo 2329 with linear regression fit and upper and lower 95% limits of agreement.**

WARNINGS

Single use devices cannot be reused. If devices are to be used again, they must be returned to Medline ReNewal for reprocessing. Please see Medline ReNewal instructions to healthcare facilities before returning.

The names of actual companies and products mentioned herein may be the trademarks of their respective owners.

Medline ReNewal Reprocessed Nellcor™ OxiMax SpO2 Sensors Models MAXA, MAXAL, MAXP, MAXI, and MAXN

Instructions for Use

Read the* Instructions for Use *in their entirety* before *using Medline ReNewal Reprocessed Nellcor™ OxiMax SpO2Sensors.

Failure to comply may result in patient and/or healthcare-staff injury.

Description:	Reprocessed device for single use. Reprocessed by Medline ReNewal.
Non Sterile:	The device is supplied non sterile.
Caution:	Federal (USA) law restricts this device to sale by or on the order of a physician.
Contact:	For more information, please call Medline ReNewal Customer Service: 1-866-866-7477.

DESCRIPTION

Medline ReNewal Reprocessed Nellcor OxiMax SpO2 Sensors. Following clinical use, each sensor is returned to Medline ReNewal where it is cleaned, disinfected, and packaged for an additional clinical use. Each sensor is tracked through the reprocessing cycle to monitor the number of times the sensor has been reprocessed.

This product cannot be adequately cleaned and/or sterilized by the user to facilitate safe reuse and is, therefore, intended for single use. Attempts to clean or sterilize these devices may result in a bio- incompatibility, infection or product failure risks to the patient. If sensors are to be used again, they must be returned to Medline ReNewal for reprocessing. Please see Medline ReNewal Instructions to Healthcare Facilities – Pulse Oximeters before returning.

This product contains DEHP. The intended use limits exposure to transient contact, minimizing the risk of DEHP release from the device. In order to avoid undue risk of DEHP exposure in children and nursing or pregnant women, product should only be used as directed.

Devices have been determined to be biocompatible following validated reprocessing methods. Inspection and pre-release testing are used to ensure appropriate device integrity and function of each device prior to release of product for use.

INDICATIONS

Medline ReNewal Reprocessed Nellcor OxiMax SpO2 Sensors are indicated for single patient use when continuous noninvasive arterial oxygen saturation and pulse rate monitoring are required for patients in the sizes indicated in the respective sensor directions for use.

The Medline ReNewal Reprocessed Nellcor OxiMax Adult SpO2 Sensor, model(s) MAXA(L) is indicated for single patient use when continuous noninvasive arterial oxygen saturation and pulse rate monitoring are required for patients weighing more than 30 kg.

The Medline ReNewal Reprocessed Nellcor Pediatric SpO2 Sensor, model MAXP is indicated for single patient use when continuous noninvasive arterial oxygen saturation and pulse rate monitoring are required for patients weighing between 10 and 50 kg.

The Medline ReNewal Reprocessed Nellcor Infant OxiMax SpO2Sensor, model MAXI is indicated for single patient use when continuous noninvasive arterial oxygen saturation and pulse rate monitoring are required for patients weighing between 3 and 20 kg.

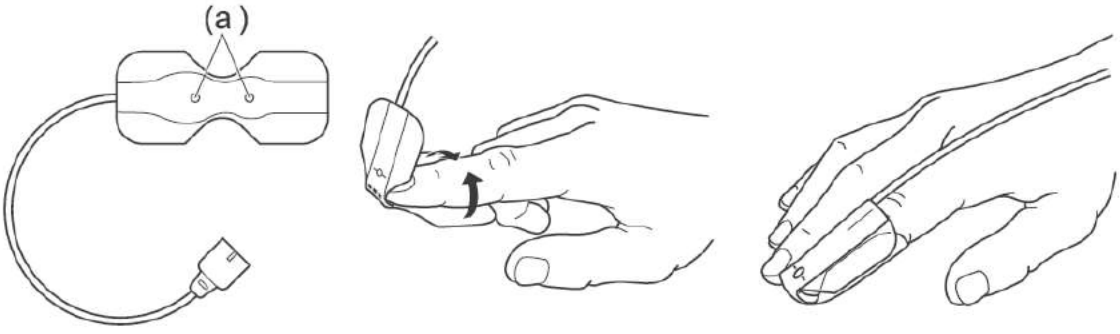
The Medline ReNewal Reprocessed Nellcor™ Neonatal/Adult SpO_2 Sensor, model MAXN is indicated for single patient use when continuous noninvasive arterial oxygen saturation and pulse rate monitoring are required for neonates weighing less than 5 kg or adults weighing more than 40 kg.

CONTRAINDICATIONS

The Medline ReNewal Reprocessed Nellcor OxiMax SpO2 Sensors are contraindicated for use on patients who exhibit allergic reactions to the adhesive tape and low-perfused patients.

INSTRUCTIONS FOR USE

Models MAXA(L) and MAXP



(1) (2) (3)

1. Remove plastic backing from the MAXA(L) or MAXP and locate transparent windows (a) on the adhesive side. Windows cover optical components. **(1)**

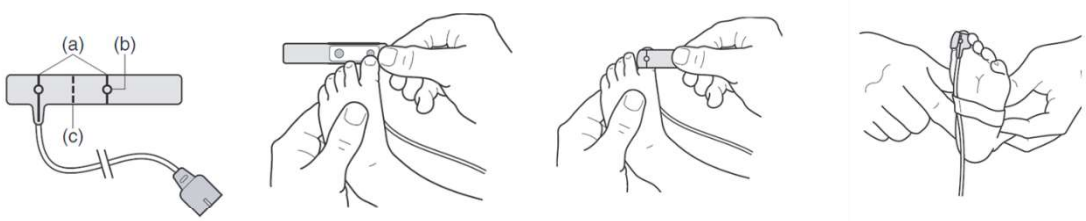
   An index finger is the preferred MAXA(L) or MAXP location. Alternatively, apply the sensor to a small thumb, smaller finger, or great toe.

***Note*:** When selecting a sensor site, priority should be given to an extremity free of an arterial catheter, blood pressure cuff, or intravascular infusion line.

2. Orient the MAXA(L) or MAXP so the dashed line in the middle of the sensor is centered on the tip of the digit. Wrap adhesive flaps on non-cable end around the digit. Note that the cable must be positioned on the top of the hand. **(2)**
3. Fold cable end over top of digit so that windows are directly opposite each other. Wrap adhesive securely around sides of digit. **(3)**
4. Plug the MAXA(L) or MAXP into the oximeter and verify proper operation as described in the oximeter operator's manual.

Note: If the sensor does not track the pulse reliably, it may be incorrectly positioned-or the sensor site may be too thick, thin, or deeply pigmented, or otherwise deeply colored (for example, as a result of externally applied coloring such as nail polish, dye, or pigmented cream) to permit appropriate light transmission. If any of these situations occurs, reposition the sensor or choose an alternate Nellcor sensor for use on a different site.

Model MAXI



1. Remove plastic backing from the MAXI and locate transparent windows (b) on the adhesive side. Windows cover optical components. Note corresponding alignment marks (a) on the non-adhesive side and dashed line (c) midway between the marks. **(1)**

   A great toe is the preferred MAXI location. Alternatively, apply the sensor to another digit of similar size, for example a thumb.

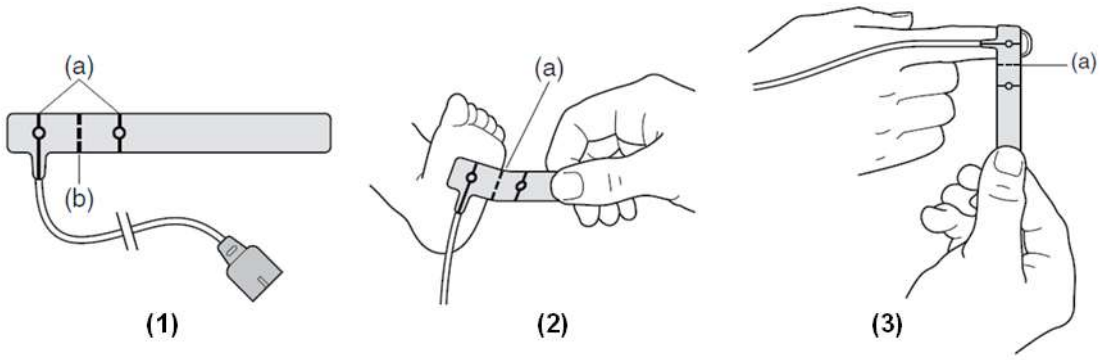
Note: When selecting a sensor site, priority should be given to an extremity free of an arterial catheter, blood pressure cuff, or intravascular infusion line.

2. Orient the MAXI so the window next to the cable is aligned on the bottom of the great toe as shown. The cable should extend towards the heel. **(2)**
3. Wrap the MAXI firmly, but not too tightly around the toe. Windows must oppose each other. **(3)**
4. Wrap any excess tape loosely around toe. Use additional tape provided to secure cable across bottom of foot, loosely enough to maintain good circulation. **(4)**

5. Plug the MAXI into the oximeter and verify proper operation as described in the oximeter operator's manual.

Note: If the sensor does not track the pulse reliably, it may be incorrectly positioned—or the sensor site may be too thick, thin, or deeply pigmented, or otherwise deeply colored (for example, as a result of externally applied coloring such as nail polish, dye, or pigmented cream) to permit appropriate light transmission. If any of these situations occurs, reposition the sensor or choose an alternate sensor for use on a different site.

Model MAXN



1. Remove plastic backing from the MAX-N and locate transparent windows (a) on the adhesive side. Windows cover optical components. Note corresponding alignment marks (a) on the non-adhesive side and dashed line (b) midway between the marks. **(1)**
2. Orient the MAXN so the dashed line is on the lateral edge of the site.

   Neonates: The preferred site is a foot. Alternatively, use a hand. The window next to the cable goes on the sole of the foot as shown. **(2)**

   Adults: The preferred site is an index finger. Alternatively, other fingers may be used. The window next to the cable goes on the nail side, distal to the first joint. Do not place on a joint. Note that the cable must be positioned on the top of the hand. **(3)**

   Note: When selecting a sensor site, priority should be given to an extremity free of an arterial catheter, blood pressure cuff, or intravascular infusion line.

3. Wrap the MAXN firmly, but not too tightly around the foot or finger. Windows must oppose each other.
4. Plug the MAXN into the oximeter and verify proper operation as described in the oximeter operator's manual.

Note: If the sensor does not track the pulse reliably, it may be incorrectly positioned—or the sensor site may be too thick, thin, or deeply pigmented, or otherwise deeply colored (for example, as a result of externally applied coloring such as nail polish, dye, or pigmented cream) to permit appropriate light transmission. If any of these situations occurs, reposition the sensor or choose an alternate sensor for use on a different site.

WARNINGS

- **Do not use the any oximetry sensors during MRI scanning. Conducted current may cause burns. Also, the sensors may affect the MRI image, and the MRI unit may affect the accuracy of oximetry measurements.**

CAUTIONS

1. Do not use if package is damaged.
2. Failure to apply the sensor properly may cause incorrect measurements.
3. While the sensor is designed to reduce the effects of ambient light, excessive light may cause inaccurate measurements. In such cases, cover the sensor with opaque material.
4. Circulation distal to the sensor site should be checked routinely. The site must be inspected every 8 hours to ensure adhesion, skin integrity, and correct optical alignment. If skin integrity changes, move the sensor to another site.
5. Intravascular dyes or externally applied coloring such as nail polish, dye, or pigmented cream may lead to inaccurate measurements.
6. Motion may compromise performance. In such cases, try to keep the patient still, or change the sensor site to one with less motion.
7. Do not immerse in water or cleaning solutions. Do not sterilize. Immersion or sterilization could damage the sensor.
8. If the sensor is wrapped too tightly or supplemental tape is applied, venous pulsations may lead to inaccurate saturation measurements.
9. Do not alter or modify the sensor. Alterations or modifications may affect performance or accuracy.
10. The operator must verify the compatibility of the monitor, sensor, and cable before use, otherwise patient injury can result.
11. Misapplication of a pulse oximeter sensor with excessive pressure for prolonged periods can induce pressure injury.
12. For additional warnings, cautions or contraindications with Nellcor pulse oximeters, refer to the instrument operator's manual or contact the manufacturer of the instrument.

ACCURACY SPECIFICATIONS

The Medline ReNewal Reprocessed Nellcor OxiMax SpO_2 Sensors are indicated for the following conditions:

- SpO_2 range: 70 – 100%
- Pulse rate: 20 – 250 bpm

- Operating temperature: 5 – 40ºC
- Storage temperature: -20 – 60ºC
- Humidity: 15-95%

Table 1 provides the specifications of Medline ReNewal Reprocessed Nellcor OxiMax SpO_2 Sensors.

Table 1: Specifications for the Medline ReNewal Reprocessed Nellcor OxiMax SpO_2 Sensors

Model Number	Sensor Type	Application Site	Saturation Accuracy (%)	Pulse Rate Accuracy (bpm)	Patient Weight (kg)
MAXA(L)	Adult Adhesive Sensor	Finger	± 2	± 3	> 30
MAXP	Pediatric Adhesive Sensor	Finger	± 2	± 3	10 – 50
MAXI	Infant Adhesive Sensor	Toe	± 2	± 3	3 – 20
MAXN	Neonatal/Adult Adhesive Sensor	Foot/Finger	± 2 in adults	± 3	< 5 kg > 40 kg

Table 2 shows the root mean square of the error (A_{RMS}) values measured using the Medline ReNewal Reprocessed Nellcor OxiMax SpO_2 Pulse Oximeter Sensors, models MAXA (adult) and MAXN (neonatal/adult), in a clinical study on adult volunteers.[1] Pulse oximeter equipment measurements are statistically distributed, only about two-thirds of pulse oximeter equipment measurements can be expected to fall within ±Arms of the value measured by a co-oximeter. A grouping strategy was used for testing and therefore two representative sensor models were utilized to obtain data. The data obtained by the sensor model MAXA represents the accuracy specifications of the MAXAL and MAXP devices and the data obtained for the sensor model MAXN represents the accuracy specifications of the MAXI devices.

All specifications were validated with the Nellcor N600x Pulse Oximeter system, which contains the NELL-1 board.

[1] Models MAXA and MAXN were included in the clinical testing to represent the breadth of the reprocessed Nellcor devices.

Table 2: Summary of accuracy data collected during the adult clinical validation study.

Model Under Test	Saturation Range (%)			
	70 – 100	90 – 100	80 – 90	70 – 80
MAXA A_{rms}[a]	1.6	1.2	1.4	2.1
MAXN A_{rms}	1.7	1.5	1.5	2.1

[a] A_{rms} = average root mean square.

Figures 1 and 2 provide graphical representation of sample data points acquired during the adult clinical trial using the Medline ReNewal Reprocessed Nellcor OxiMax SpO2 Sensors.

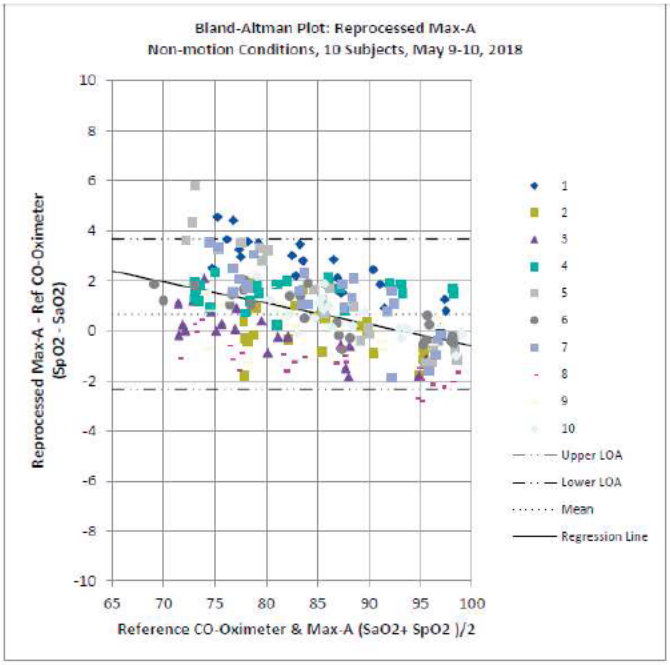


Figure 1: Bland-Altman plot of all sampled data points by subject for the adult clinical study for the Medline ReNewal Reprocessed Nellcor MAXA sensor with linear regression fit and upper and lower 95% limits of agreement.

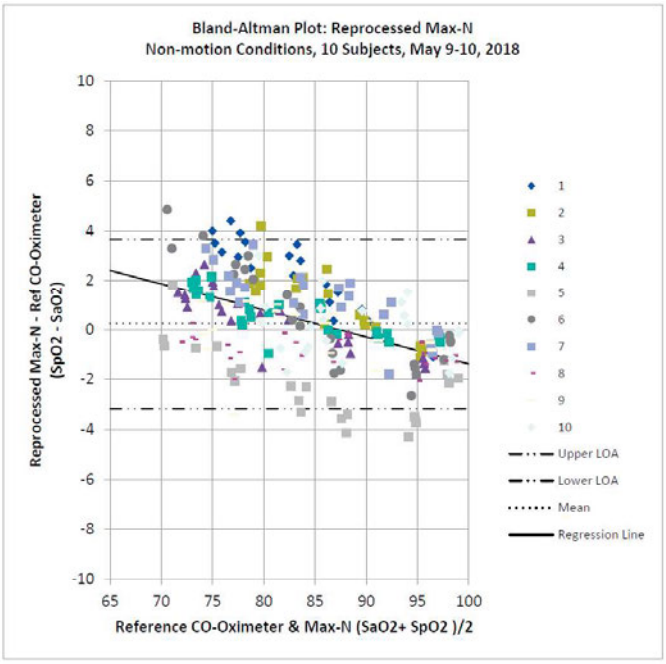


Figure 2: Bland-Altman plot of all sampled data points by subject for the adult clinical study for the Medline ReNewal Reprocessed Nellcor MAXN sensor with linear regression fit and upper and lower 95% limits of agreement.

WARNINGS

Single use devices cannot be reused. If devices are to be used again, they must be returned to Medline ReNewal for reprocessing. Please see Medline ReNewal Instructions to Healthcare Facilities – Pulse Oximeters before returning.

The names of actual companies and products mentioned herein may be the trademarks of their respective owners.

Consult Instructions for Use

Non-sterile

Do not re-use. Single patient use only

Not made with natural rubber latex

Do not use if package is damaged

Contains DEHP