September 4, 2020

Innovision ApS
% H. Jenkins
Regulatory Affairs Consultant
Wood Burditt Group
10 E. Scranton Ave., Ste. 201
Lake Bluff, Illinois 60044

Re: K190561
Trade/Device Name: Nicu V'02
Regulation Number: 21 CFR 868.1730
Regulation Name: Oxygen Uptake Computer
Regulatory Class: Class II
Product Code: BZL
Dated: July 31, 2020
Received: August 3, 2020

Dear H. Jenkins:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Todd Courtney
Assistant Director
DHT1C: Division of ENT, Sleep Disordered
Breathing, Respiratory and
Anesthesia Devices
OHT1: Office of Ophthalmic, Anesthesia,
Respiratory, ENT and Dental Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K190561

Device Name
NICU V'O2

Indications for Use *(Describe)*

The device is indicated for use in mechanically ventilated neonate, infant and pediatric patients where the precise and direct measurement of oxygen uptake (V'O2), carbon dioxide excretion (V'CO2), resting energy expenditure (REE) and respiratory quotient (RQ) will allow the attending physician to plan and monitor an optimal nutrition regime for the patient in terms of substrate composition and utilization.

Applications

The NICU V'O2 device is a non-invasive indirect calorimeter for use in clinical and/or research applications for determination of metabolic parameters by measuring expired gas composition (oxygen and carbon dioxide) and volume.

The device is intended for use by qualified medical staff in professional healthcare facilities.

Population studied

Clinical testing has been performed in intubated, mechanically ventilated neonates and infants with ability to tolerate brief interruptions in the ventilatory circuit when connecting and disconnecting the device.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

1. Applicant Information

Name:	COSMED Nordic ApS
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Contact person(s):	Peter Clemensen (CEO - Nordic) - pc@cosmed.com
	Karen Hvid Ipsen (Director QA/RA - Nordic) - ki@cosmed.com
Type of Submission:	Traditional 510(k)
Submission Number:	K190561
Date of preparation:	February 22, 2019
Date of revision:	August 27, 2020
Submitter (US Agent):	The Wood Burditt Group
	10 E. Scranton Ave., Suite 201
	Lake Bluff, IL 60044
	(847) 234-7500
	Contact person: H. Carl Jenkins – hcjenkins@woodburditt.com

2. Device Name and Classification

Trade Name:	NICU V'O2
Common or Usual Name:	Indirect calorimeter
Regulatory Class:	Class II
Classification Name:	Oxygen uptake computer
	(21 CFR 868.1730, Product Code BZL. Panel: Anesthesiology)

3. Identification of Legally Marketed Predicate Devices

Primary Predicate

Device:	MedGraphics Express Series
Manufacturer:	Medical Graphics Corporation (Now MGC Diagnostics)
510(k) number:	K070858

Secondary Predicate No. 1

Device:	Innocor (incl. Cardiopulmonary Exercise Testing Option)
Manufacturer:	Innovision ApS (same as applicant)
510(k) number(s)	K051907, K071911 and K083879

Secondary Predicate No. 2

Device:	REEVUE Indirect Calorimeter (Model: 8100)
Manufacturer:	KORR Medical Technologies, Inc.

510(k) number: K021490

Reference method

Device: Douglas Bag (Gold Standard)[1]
Manufacturer: N/A
510(k) number N/A

4. Device Description

The NICU V'O2 device is an indirect calorimeter that allows accurate and precise quantification of oxygen consumption ($V'O_2$), carbon dioxide excretion ($V'CO_2$), resting energy expenditure (REE, the number of calories consumed per day) and respiratory quotient (RQ, the ratio of $V'CO_2$ to $V'O_2$) in mechanically ventilated patients. Patients include neonate, infant and pediatric patients with a body weight from 0.5 kg, low minute ventilation, high respiratory rate, and receiving fluctuating and/or elevated inspiratory oxygen concentrations.

The device functions by measuring oxygen concentration (using laser diode sensor technology) and carbon dioxide concentration (using NDIR infrared sensor technology) in inspired and expired gas as well as inspiratory flow. The inspiratory flowmeter (differential pressure type pneumotach) is attached at the patient inspiratory outlet of the ventilator. An inspiratory gas sample line is connected to the inspiratory limb of the patient breathing circuit, and an expiratory gas sample line is connected to the ventilator exhaust. The device automatically alternates between these two sample points.

Oxygen consumption is determined by comparing the amounts of oxygen in inspired and expired gas, and carbon dioxide excretion is determined by comparing the amounts of carbon dioxide in expired and inspired gas, respectively, per unit of time. These amounts are calculated from the primary measurements of oxygen and carbon dioxide concentrations and gas flow.

The resting energy expenditure (or resting metabolic rate), which is defined as the number of calories the body expends daily during resting conditions, is calculated from the values of oxygen consumption and carbon dioxide excretion using the modified Weir equation:

$$REE = (V'O_2 \times 3.941 + V'CO_2 \times 1.106) \times 1440 \ \frac{kcal \cdot min}{day \cdot L}$$

Respiratory Quotient is calculated as the ratio of carbon dioxide produced by the patient to oxygen consumed by the patient.

[1] Initially described by Gordon Douglas in Proceedings Of The Physiological Society, March 18, 1911 "A method for determining the total respiratory exchange in man".
Reviewed e.g. by Shephard, Eur J Appl Physiol (2017) 117:381–387: "Open-circuit respirometry: a brief historical review of the use of Douglas bags and chemical analyzers".

The duration of measurement can be from tens of minutes to 24 hours, partly because the inspiratory flowmeter only sees dry gas and therefore does not significantly change calibration over time.

The device consists of two main components. An analyzer unit to which the patient is connected via gas sample and flowmeter pressure lines, and a computer running the dedicated software application under the Windows operating system. The software application works in conjunction with the hardware, and the computer presents in real time measured signals and computed physiological parameters, both as numeric and graphical data. The computer is the main control interface for the ICU staff using the device and offers options for offline data management.

The device is powered through an external medical AC/DC power supply.

5. Indications for Use Statement

The device is indicated for use in mechanically ventilated neonate, infant and pediatric patients where the precise and direct measurement of oxygen uptake ($V'O_2$), carbon dioxide excretion ($V'CO_2$), resting energy expenditure (REE) and respiratory quotient (RQ) will allow the attending physician to plan and monitor an optimal nutrition regime for the patient in terms of substrate composition and utilization.

Applications

The NICU V'O2 device is a non-invasive indirect calorimeter for use in clinical and/or research applications for determination of metabolic parameters by measuring expired gas composition (oxygen and carbon dioxide) and volume.

The device is intended for use by qualified medical staff in professional healthcare facilities.

Population studied

Clinical testing has been performed in intubated, mechanically ventilated neonates and infants with ability to tolerate brief interruptions in the ventilatory circuit when connecting and disconnecting the device.

6. Comparison of Technological Characteristics

MedGraphics Express Series Equivalence

The MedGraphics Express Series (MedGraphics device) has been chosen as primary predicate because of similarities to the new NICU V'O2 device in its intended use/indications for use. They are both intended for indirect calorimetry and determination of metabolic parameters for nutritional assessment of ventilated patients. They both measure oxygen consumption ($V'O_2$) and carbon dioxide excretion ($V'CO_2$) and compute the respiratory quotient (RQ) and the resting energy expenditure (REE) using the Weir equation. The MedGraphics device may also be used for spontaneously breathing patients contrary to the NICU V'O2. There are also minor technological dissimilarities in the oxygen sensor type used to determine O_2 concentrations and in gas collection principles in the two devices. These differences are covered by the secondary predicates.

Innocor Model INN00010 Predecessor Device Equivalence

The Innocor Model INN00010 (Innocor device) actively marketed in the US by applicant as a CPX system has been included as a secondary predicate both for the indications for use which include measurements of $V'O_2$, $V'CO_2$ and RQ and because the oxygen sensor technology and flow measurement principle in this legally marketed device are identical to those of the new NICU V'O2 device. Like the primary predicate, Innocor uses the breath-by-breath gas exchange method. Innocor has not been selected as the primary predicate since it is not intended for ventilated patients or neonates/infants and does not compute REE from the metabolic parameters.

REEVUE Indirect Calorimeter Equivalence

The REEVUE Indirect Calorimeter (REEVUE device) has been selected as an additional secondary predicate because of similarities in intended use/indications for use and technologies, and to demonstrate that the mixing box principle has been applied instead of the breath-by-breath principle for an indirect calorimeter that is legally marketed. This device, however, does not measure CO_2 as do the other predicates but instead assumes a constant RQ (ratio of $V'CO_2$ to $V'O_2$). Besides, the REEVUE device is only indicated for spontaneously breathing patients where supplementary oxygen is not being given.

Reference method

The Douglas Bag, where expired gas from the patient is collected in a non-diffusing gas bag over time and subsequently analyzed for volume and composition, is considered the gold standard for respiratory gas exchange and hence estimation of energy expenditure (indirect calorimetry). It has been included as a reference method because, in addition to bench testing, it has been used to validate the NICU V'O2 in an animal model and in a clinical performance test in patients.

Substantial Equivalence Comparison Matrix / Summary of Technological Characteristics

The technological characteristics of the new NICU V'O2 device are compared to those of the predicate devices below. Intended use/indications for use are based on the 510(k) summaries for the devices, whereas data on technological characteristics is obtained partly from product information from product data sheets and websites etc.

Specification	**Subject device**	**Predicate Devices**		
	NICU V'O2	**Primary** **MedGraphics Express**	**Secondary No. 1** **Innocor INN00010**	**Secondary No. 2** **REEVUE IC**
510(k) Number	Proposed device	K070858	K071911	K021490
Product code	BZL	BZL	BZL DQK	BZL
Class	Class II	Identical	Identical	Identical
Intended Use	**Indirect calorimetry**	**Indirect calorimetry & cardiopulmonary function testing**	**Cardiopulmonary function testing**	**Indirect calorimetry**

Specification	Subject device	Predicate Devices		
	NICU V'O2	**Primary** **MedGraphics Express**	**Secondary No. 1** **Innocor INN00010**	**Secondary No. 2** **REEVUE IC**
	The NICU V'O2 device is a non-invasive indirect calorimeter intended for use in clinical and/or research applications for determination of metabolic parameters by measuring expired gas composition (oxygen and carbon dioxide) and volume.	MedGraphics Express Series is intended for medical applications requiring a non-invasive assessment of the cardiopulmonary response to exercise or measurement of energy expenditure using indirect calorimetry.	Innocor's cardiopulmonary exercise testing option is intended to measure oxygen uptake (metabolic rate) and related parameters to objectively and non-invasively assess cardiac and pulmonary function at rest and during exercise.	The device is intended for use in clinical and research applications to measure oxygen uptake.
Target patient population	Neonate to pediatric. Mechanically ventilated.	No documentation contained in 510(k) summary. Inferred from datasheet: Pediatric to adult. Mechanically ventilated and spontaneously breathing.	Pediatric to adult. Spontaneously breathing.	Pediatric to adult Device not compatible with mechanical ventilation or patients on supplemental oxygen.
Target users	Prescription use only.	Identical	Identical	Identical
Patient interface	No patient contact. Distal sensors inserted in breathing circuit.	No patient contact (in mechanical ventilation mode). Proximal sensors.	Mouthpiece or mask. Proximal sensors.	Mouthpiece or mask. Proximal unidirectional breathing valves and distal sensors.
Parameters	$V'O_2$ $V'CO_2$ RQ REE	Identical	$V'O_2$ $V'CO_2$ RQ REE not calculated	$V'O_2$ $V'CO_2$ not determined RQ not determined REE
Operating principle	Mixing box / Inspiratory flow measurement Inspiratory and expiratory O_2 and CO_2 measurement (Side-stream) REE: Modified Weir Equation using measured O_2 and CO_2.	Breath-by-breath / Proximal flow measurement Proximal O_2 and CO_2 measurement (Side-stream) No documentation contained in 510(k) summary.	Breath-by-breath / Proximal flow measurement Proximal O_2 and CO_2 measurement (Side-stream) REE not calculated.	Mixing box / Expiratory flow measurement Expiratory O_2 measurement (Side-stream inside of equipment). Ambient (inspired) O_2 concentration assumed 20.93%. Similar – However, CO_2 not measured. REE calculation based on assumed RQ of 0.83.
Oxygen sensor specification:	Laser diode absorption spectroscopy	Galvanic cell	Laser diode absorption spectroscopy	Galvanic fuel cell

Specification	Subject device	Predicate Devices		
	NICU V'O2	**Primary** MedGraphics Express	**Secondary No. 1** Innocor INN00010	**Secondary No. 2** REEVUE IC
Carbon dioxide sensor specification:	Non-dispersive IR spectroscopy	Non-dispersive IR spectroscopy	Photoacoustic IR spectroscopy	None
Flow sensor specification:	Type: Differential pressure pneumotach (Mesh screen type)	Type: Differential pressure pneumotach (Bidirectional pitot tube)	Type: Differential pressure pneumotach (Mesh screen type)	Type: Differential pressure pneumotach (Fixed orifice)
Clinical	Validated by bench testing, in an animal model and in patients. Reference method: Douglas bag.	No data submitted.	Validated by bench testing.	Validated by bench testing and in patients. Reference method: Douglas bag.

7. Non-Clinical Performance Data to Establish Equivalence

The NICU V'O2 device has been thoroughly tested through non-clinical performance testing and validation that establishes equivalence. The following validation testing was applied to the development of the system as summarized in the following: Performance verification against bench top simulator and animal comparative testing.

Bench Testing

A comprehensive in vitro performance test was conducted to determine the accuracy of the $V'O_2$ and $V'CO_2$ measurements and derived parameters at varying $V'O_2$ and ventilator settings.

A lung simulator was used as a reliable reference technique (gold standard) to quantitatively establish accuracy and reliability of the device. In this technique, simulated $V'O_2$ and $V'CO_2$ can be varied by infusion of a certified gas mixture (50% O_2/50% CO_2) into an artificial lung circuit (silicone bellows) at a constant rate, comparing measured with simulated $V'O_2$ and $V'CO_2$ within a matrix of varying metabolic rate, tidal volume (peak pressure above PEEP), respiratory rate, and fraction of inspired oxygen (F_IO_2, normoxic and hyperoxic mixtures). Respiratory parameters were changed via settings on an infant ventilator driving the lung simulator.

Infusion was provided by means of a mass flow controller.

As the volumetric flow rate of CO_2 from the test gas directly represents true $V'CO_2$ at standard temperature and pressure, it can be assessed how accurately the measured $V'CO_2$ resembles the known reference flow. Similarly, a precisely-known flow of O_2 (with zero N_2 content) is utilized to simulate a negative $V'O_2$ (i.e. O_2 production). Since the CO_2 and O_2 fractions in the test gas are chosen to be equal, the reference RQ is equal to -1.

In conclusion, bench testing has shown that this device can measure $V'O_2$, $V'CO_2$ and derived RQ and REE with <15% error within the neonatal size range, and functions well up to respiratory rates of 60-80 BPM and F_IO_2 of 0.7.

The in vitro validation has been published in the peer-reviewed article:

Nachman et al. A device for the quantification of oxygen consumption and caloric expenditure in the neonatal range. Anesth Analg 2018;127:95–104.

Animal Testing

An in vivo performance test was conducted in animals to determine the accuracy of the $V'O_2$ and $V'CO_2$ measurements and derived parameters at respiratory variables reflective of those present in Sprague-Dawley rats on mechanical ventilation using a clinical ventilator. Douglas bag gas collection was used as reference technique.

In conclusion, the device has been demonstrated to exhibit clinically acceptable bias and precision in $V'O_2$, $V'CO_2$, RQ and REE in vivo in animals under low minute ventilations.

There were no procedure related complications in the animal study.

The animal validation has been published in the peer-reviewed article:

Nachman et al. A device for the quantification of oxygen consumption and caloric expenditure in the neonatal range. Anesth Analg 2018;127:95–104.

8. Clinical Performance Data to Establish Equivalence

An in vivo performance test was conducted in newborn patients on an infant ventilator to determine the accuracy of the $V'O_2$ and $V'CO_2$ measurements and derived parameters. Douglas bag gas collection was used as reference technique.

In conclusion, the device has been demonstrated to exhibit clinically acceptable bias and precision in $V'O_2$, $V'CO_2$, RQ and REE in patients under low minute ventilations and high respiratory rates. The bias in $V'O_2$ and $V'CO_2$ were +0.22 mL/kg/min and +0.033 mL/kg/min, respectively, corresponding to a mean percentage error (i.e. discrepancy between device and reference) of approximately 3%.

No procedure related adverse effects or complications were observed in the clinical study.

The clinical validation has been published in the peer-reviewed article:

Nachman et al. A device for the quantification of oxygen consumption and caloric expenditure in the neonatal range. Anesth Analg 2018;127:95–104.

9. Substantial Equivalence Conclusion

The NICU V'O2 device meets the functional claims, product specifications and intended use as described in the product labeling.

The performance of the NICU V'O2 device was evaluated by a combination of bench testing, animal testing and a clinical study in order to make the validation as comprehensive as possible and at the same time limit the number of tests on patients required to support substantial equivalence.

An accuracy of 20% (determined as the difference between device and reference measurements or simulator) was considered clinically acceptable. The results indicated that the device meets or exceeds the pass criteria for each test. The device can measure $V'O_2$, $V'CO_2$, RQ and REE

with sufficient accuracy for clinical decision-making within the neonatal to pediatric size range, including in the setting of tachypnea or hyperoxia.

Based on its underlying technology and on performance as documented in the bench tests, animal tests and clinical trial, Innovision concludes that the NICU V'O2 device is substantially equivalent to the predicate devices described in the submission that are currently legally marketed for the same intended use.