	CLINICAL EVALUATION REPORT	CER_EO-150	
		Version	I
		Date	23/02/2023

COMPANY NAME

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Research and development
Quality and Regulatory affairs

PRODUCT

EO-150 ventilator

DOCUMENT TITLE

100_66 rev I : CLINICAL EVALUATION REPORT_EO 150 ventilator

DOCUMENT MANAGEMENT

Version	Date	Modifications	Written by:	Reviewed by:	Approved by:
A to F	-	Initial MDR submission of CER (See previous document 100-66)	-	-	-
G	28/06/2022	MDR CER submission in response to GMED audit NC 17/21 – 17/02/2022. NCs GMED report P603936-P1 04/02/2022	Sarah RENAUD, Consultant (EFOR Group)	Katharina HOEGL, Technical Specialist and Charlotte BENOIT, Head of Clinical Department (EFOR Group)	Patrick DEHOUR, Director QA&RA, (EOVE)
H	28/10/2022	CER update according to the technical file EO-150 rev I and user manual rev DE	Sarah RENAUD, Consultant (EFOR Group)	Katharina HOEGL, Technical Specialist and Charlotte BENOIT, Head of Clinical Department (EFOR Group)	Patrick DEHOUR, Director QA&RA, (EOVE)

I	23/02/2023	CER update concerning the non-conformities NC F/06 ; NC C/11 of the GMED report RDM-CEAR EOVE P603936_P2. Modification of §3.5; 3.7.3 ; 3.10.4.7 ; 8.3 ; 8.3.3 regarding the patient benefits	Sarah RENAUD, Consultant (EFOR Group)	Katharina HOEGL, Technical Specialist and Charlotte BENOIT, Head of Clinical Department (EFOR Group)	Patrick DEHOUR, Director QA&RA, (EOVE)

SIGNATURES

	Name and Function	Date	Signature
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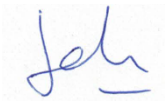
Reviewer	Charlotte BENOIT, Head of Clinical Department (EFOR Group)	23/02/2023	
Reviewer	Jean LE ROUX, Pilot process Marketing & clinical (EOVE)	23/02/2023	
Reviewer	Cédric JOURDAIN, Director R&D, (EOVE)	23/02/2023	
Approver	Patrick DEHOUR, Director QA&RA (EOVE)	23/02/2023	

1 SUMMARY

The current Clinical Evaluation Report (CER) evaluates the **EO-150 ventilator**, which is a medical device European Conformity (CE) marked by EOVE. This report is written to update the previous CER version of these medical devices according to the Medical Device Regulation MDR 2017/745 and to fulfil MEDDEV 2.7/1 rev. 4 guideline requirements. The clinical evaluation plan (CEP) (“**100_66 rev H : CEP_EO-150”**) is defined by EOVE and covers the **EO-150 ventilator** as well as its commercial variants namely, MV-150 and VEMO150. Hence, the term “**EO-150 ventilator**” refers to the references EO-150VNT, EO-150VEMO and MV-150VNT.

The **EO-150 ventilator** is CE-marked since 2015. According to Rule 12 of Annex VIII of MDR 2017/745, the **EO-150 ventilator** is a class IIb Medical Device that is not in direct contact with the patient. Therefore, the benefits to patients are indeed indirect; as the direct benefits are attributed to the air or gas/air blend administered to the patient.

The **EO-150 ventilator** is an artificial respirator that provides ventilatory support for patients with acute or chronic respiratory failure. This device is mainly intended to be used at the patient's home. It is initially installed by a healthcare provider who has been mandated by a doctor to set up the patient's equipment. The provider performs an initial manipulation during installation and then returns regularly to ensure patient follow-up. Visits are frequent at the beginning of the treatment and are limited to maintenance operations when the patient has stabilised.

The operation of the ventilator is based on a closed-loop control system of the turbine speed, on the pressure or airflow rate set points. The device has two operating modes, barometric mode (pressure control) or volumetric mode (airflow control). It can also work in a dual circuit with a dedicated expiratory valve and sensor. The **EO-150 ventilator** offers a configuration to provide single circuit leakage ventilation.

In accordance with the demands and expectations of MEDDEV 2.7/1 rev. 4, this CER includes a section dedicated to the State of the Art. The data sets included in this section have been identified and selected according to current standards (MEDLINE, Cochrane). Of the 356 data sets initially identified through systematic literature searches, 130 were included in the State of the Art, and of those 29 were used to demonstrate the performance and security of home mechanical ventilators.
The State of the Art showed that:

- HMV is based on the well-established and documented technology of artificial ventilation by positive pressure dating back to the 1960’s.
- HMV can be applied for many indications (chronic obstructive pulmonary disease (COPD), neuromuscular disorders (NMDs), obesity hypoventilation syndrome (OHS)…) but more generally for the treatment of patients of all ages with respiratory failure.
- Long term HMV is safe for adults but there is limited data for paediatric patients which needs to be further strengthened.
- Chronic and long-term use of MV is increasingly prescribed thus, HMV is in line with modern medical needs with regards to respiratory failure. Hence, the number of patients prescribed HMV, both short- and long-term is increasing globally. The most common indications for HMV are COPD, NMDs, OHS, chest wall disorders (CWDs).
- Today MV offers multiple ventilation modes to better suit patient needs.
- HMV initiation seems possible in both a hospital and home setting with no damaging effects on patient outcome and health. In fact, this approach seems beneficial for both the patient, with faster MV implementation, and the healthcare system as it is more cost-effective, frees up hospital resources and medical staff time.
- HMV implementation and telemedicine suggest the need to set up other resources such as on-call medical staff available to assist and intervene upon incident occurrence.

It has been described that HMV offers benefits such as improved survival, transcutaneous carbon dioxide levels ($PtCO_2$), Partial pressure of carbon dioxide in arterial blood ($PaCO_2$) levels, quality of life (QoL), better overall

therapy comfort, improved respiratory compliance and lowers costs, needs for invasive ventilation (IV) as well as exacerbation frequency for COPD patients.

- HFNC therapy is reportedly better tolerated, improves $PaCO_2$ levels and also decreases respiratory rate (RR), length of stay in intensive care/hospital and exacerbation frequencies (COPD) compared to conventional ventilation therapy. Although often considered louder, overall comfort was deemed better with HFNC therapy.
- The assessments of health-related quality of life (HRQL) have improved but are not consistently carried out.
- High-flow oxygen therapy is increasingly prescribed for severe acute respiratory failure in diseases such as COPD exacerbations and COVID-19 infection.
- In the case of Acute Hypoxemic Respiratory Failure (AHRF), prediction of HFNC therapy failure can be strongly correlated to the ROX index and the ratio of oxygen saturation (SpO_2) to RR.
- Further data regarding HMV and HFNC therapy performance is needed as evidence is often considered of low to moderate certainty.
- Reported adverse events are generally linked to the MV itself and not specifically the ventilators. The most common adverse events for HMV are considered non-serious and outweighed by the benefits of mechanical ventilation (MV): discomfort, oro-nasal dryness and skin lesions.
- Reported side effects of HFNC therapy are discomfort linked to heat or thoraco-cervical discomfort as well as varying levels of consciousness.
- There is a need for more clear-cut international consensus around HMV practises and patient typology for better stratification.

Medical devices must demonstrate compliance with the requirements of MDR 2017/745. The requirements and obligations of manufacturers are described in Chapter I of Annex I of Regulation 2017/745. The MDR specifies that this demonstration of conformity with the general safety and performance requirements is based on a clinical evaluation as specified in Article 61.
According to Section 2 of Chapter I of MDR 2017/745, clinical evaluation is the analysis of "information relating to the safety or performance obtained in the use of a device from the following sources ...":

- the clinical investigation(s) of the device concerned,
- the clinical investigation(s) or other studies cited in scientific publications of a device whose equivalence to the device concerned can be demonstrated,
- reports in peer-reviewed scientific publications on any other clinical experience with the device concerned or with a device whose equivalence to the device concerned can be demonstrated,
- clinically relevant information from post-market surveillance (PMS), in particular post-market clinical monitoring;".

However, Section 61, paragraph 10 of Chapter VI of MDR 2017/745 states: *Without prejudice to paragraph 4, where compliance with the general safety and performance requirements is considered not to have been satisfactorily demonstrated by clinical data, an appropriate justification shall be provided for any such exceptional case based on the results of the manufacturer's risk management and review of detailed data relating to the interaction between the device and the human body, the expected clinical performance and the manufacturer's claims. In this case, the manufacturer shall duly justify in the technical documentation referred to in Annex II why he considers adequate a demonstration of compliance with the general safety and performance requirements based solely on the results of non-clinical test methods, such as technical performance evaluation, bench testing and pre-clinical evaluation.*

This justification enables the writing of a clinical evaluation without clinical performance data. The demonstration of compliance is made with the General Safety and Performances Requirements (GSPR) detailed in Annex I of MDR 2017/745:

- GSPR1: Requirement on safety and performances;
- GSPR2: Requirement on benefit/risk ratio;

- GSPR4: Requirement on safety. Adherence to the specific instructions provided with the device is essential to eliminate or mitigate the identified risks associated with the use of the device on the intended site;
- GSPR8: Any undesirable side-effect constitutes an acceptable risk when weighed against the intended performances.

Since the manufacturer EOVE claims solely technical performances for the **EO-150 ventilator**, the demonstration of device performance and safety is based on:

- A complete State of the Art;
- A description of the risks associated with the use of the medical device;
- Vigilance data, curated data (risk analysis and data from international vigilance databases);
- Compliance to non-clinical elements of common specifications considered relevant to device safety and performance, if applicable;
- Pre-clinical and bench testing / compliance to harmonised standards, if applicable;
- Post-Market Clinical Follow-up (PMCF) data.

Sales volume on the 31st December 2021, since market launch on the 15th June 2015, is 7778 **EO-150 ventilators** in total (90% of sales are in Europe). PMS activities for the **EO-150 ventilator** from EOVE have shown that between June 2015 and December 2021, 153 complaints were reported. This translates into an incidence frequency of 2%. Importantly, the frequency of complaints over the years has consistently decreased, meaning that fewer risks remain, that corrective actions are efficient and that the device and the accompanying user documentation are continuously improved in terms of patient safety. Moreover, none of these incidents had an impact on patients' health. Vigilance data regarding cybersecurity preventative measures for the device were reported by the manufacturer. In addition, a search in the international medical device vigilance databases showed a number of vigilance incidents regarding similar devices. These risks were either "one-off" unique events, specific to the similar device in question (software/firmware issues, manufacturing errors etc.) or already known to EOVE and taken into account in the risk analysis and user/patient documentation.

Cross-analysis of the literature, current information supplied with the device, risk analysis, PMS/Periodic safety update reports (PSUR) with the results of vigilance data showed that:

- **EO-150 ventilator** is compliant with the general safety, clinical performance and benefit risk profile requirements of the MDR 2017/745 and MEDDEV 2.7/1 rev. 4, including requirements regarding the design and manufacture of the devices, as well as requirements regarding the information supplied with the devices;
- The safety of the medical device was supported by preclinical tests, PMS/PSUR data on the medical device under evaluation and materiovigilances on similar medical devices;
- The performances claimed by EOVE were supported by preclinical data;
- Given the benefit-risk profile of the **EO-150 ventilator**, the risks associated with the use of the device are acceptable;
- Reported adverse events are well-known and mostly manageable as the health of the patient was not significantly impacted, if at all. The most common adverse event reported is linked to defective equipment (software/firmware bugs) or symptoms involving the skin, eyes, nose/mouth, gastrointestinal area and intolerance of the device/mask. These identified risks have been evaluated by risk analysis.
- The results of the risk analysis and its updates show that the overall residual risk is acceptable. Based on analysis and scientific knowledge, all identified risks and their mitigation measures are acceptable in relation to the benefit provided by the device.
- The risk management report shows that an adequate risk management plan has been implemented, that the residual risks and overall residual risk are acceptable, and that adequate measures are taken to monitor production and the devices installed.

- Accompanying documents for the **EO-150 ventilator** include the information needed to clearly identify the target population, inform the user of the risks associated with the use of this medical device and the means to be used to master them.

According to the CEP("**100_66 rev H : CEP_EO-150**") and the internal standard operating procedure (SOP), the next general update of this CER will be conducted in 2 years (in 2024).
The following table allows to confirm whether all requirements of the guideline MEDDEV 4.2/1 Rev 4 have been treated.

MEDDEV CHECKLIST	INCLUDED			Section in CER
Can the report be read and understood by a third party, does it provide sufficient detail for understanding the data that are available, all assumptions made, and all conclusions reached?	Yes ☒	No ☐	NA ☐	NA
If clinical data have been generated and are held by the manufacturer, are all data mentioned and adequately summarised in the report?	Yes ☐	No ☐	NA ☒	NA
If equivalence is claimed:				
Is demonstration of equivalence included in the report?	Yes ☐	No ☐	NA ☒	NA
Does the report disclose all the differences between the device under evaluation and the equivalent device?	Yes ☐	No ☐	NA ☒	NA
Does it explain why the differences are not expected to affect the clinical performance and clinical safety of the device?	Yes ☐	No ☐	NA ☒	NA
If the product is already in the market in Europe or elsewhere, has the latest PMS-PSUR / PMCF data been taken into consideration and has it been summarised and referenced in the report?	Yes ☒	No ☐	NA ☐	Section 3.3 Section 10
In respect to current knowledge/ the State of the Art:				
Has the report been updated?	Yes ☒	No ☐	NA ☐	Section 1
Is current knowledge/ the State of the Art summarised in the report and is it adequately substantiated by literature?	Yes ☒	No ☐	NA ☒	Section 0 Section 3.10
Does the content of the report fully correspond to current knowledge/ the State of the Art?	Yes ☒	No ☐	NA ☐	Section 3.10
Does the report explain why the benefit/risk profile and the undesirable side-effects are acceptable in relation to current knowledge/ the State of the Art?	Yes ☒	No ☐	NA ☐	Section 8
If the report covers several models/ sizes/ settings and/or different clinical situations, is there sufficient clinical evidence and are the report's conclusions correct for:				
All the devices?	Yes ☐	No ☒	NA ☐	NA
All its sizes, models and settings? (Including the smallest/ largest size, highest/ lowest dose, etc.)	Yes ☒	No ☐	NA ☐	Section 2
Every medical indication? (As described in the IFU/ not excluded with contraindications in the IFU)	Yes ☒	No ☐	NA ☐	Section 3
The entire target population? (From pre-term infants to old age, for males and females, etc., if not restricted in the IFU)	Yes ☒	No ☐	NA ☐	Section 3
Every form, stage and severity of the medical condition, as applicable? MEDDEV 2.7/1 revision 4 page 56 of 65 (including the most severe/ most benign forms, acute/ chronic stage, if not excluded in the IFU)	Yes ☒	No ☐	NA ☐	Section 3
All intended users? (Including lay persons, if not excluded in the IFU, and any unusual user group)	Yes ☒	No ☐	NA ☐	Section 3

MEDDEV CHECKLIST	INCLUDED			Section in CER
The whole duration of product use, including the maximal number of repeated exposure? (As allowed by the IFU)	Yes ☒	No ☐	NA ☐	Section 3
If there are any discrepancies as to the above, are they identified in the report's conclusions?	Yes ☒	No ☐	NA ☐	Section 9
Is conformity to each of the relevant general safety and performance requirements of the MDR 2017/745 clearly stated and are all discrepancies identified in the report's conclusions?	Yes ☒	No ☐	NA ☐	Section 8
Do the information materials supplied by the manufacturer correspond with the contents of the report and are all discrepancies identified in the report's conclusions?	Yes ☒	No ☐	NA ☐	Section 8 and Section 9
Do the report's conclusions identify all residual risks and uncertainties or unanswered questions that should be addressed with PMS-PSUR / PMCF studies?	Yes ☒	No ☐	NA ☐	Section 8
Is the report dated?	Yes ☒	No ☐	NA ☐	First page
Is the qualification of the evaluators included in the report and correct?	Yes ☒	No ☐	NA ☐	Section 1 and Appendix 1
Does the manufacturer hold a CV and declaration of interests of each of the evaluators and are these up-to-date?	Yes ☒	No ☐	NA ☐	Appendix 1 and Appendix 2

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ACRONYMS AND ABBREVIATIONS

FFS: Full Facial Masks
IA: Inspiratory Assist
MA: Meta-Analysis
RV: Residual Volume
SR: Systematic Review
(A)PCV: Pressure assisted/Controlled Ventilation
(A)VCV: Volume Assisted Controlled Ventilation
6MWD: 6-minute walk distance test
ABG: Arterial Blood Gases
AECOPD: Acute Exacerbation of COPD
AFQRP : Aussi Faible Que Raisonnablement Possible
AHRF: Acute Hypoxemic Respiratory Failure
ALS: Amyotrophic Lateral Sclerosis
AMD: Adjusted Mean Difference
ANSM: Agence Nationale de Sécurité du Médicament (France)
ANVISA: Health Regulatory Agency (Brazil)
APACHE: Acute Physiology and Chronic Health Evaluation
APAP: Auto-adjusted CPAP
BfArM : The Federal Institute for Drugs and Medical Devices (Germany)
BiPAP (or BPAP): Bilevel Positive Airway Pressure
BMI: Body Mass Index
BURR: BackUp Respiratory Rate
CCQ: Clinical COPD Questionnaire
CE: European Conformity
CEP: Clinical Evaluation Plan
CER: Clinical Evaluation Report
C-Flow: Continues Flow
CHRF: Chronic Hypercapnic Respiratory Failure
CI: Confidence Interval
COPD: Chronic Obstructive Pulmonary Disease
COT: Conventional Oxygen Therapy
COVID-19: Coronavirus Disease-19
CPAP: Continuous Positive Airway Pressure
CRF: Chronic Respiratory Failure
CWD: Chest Wall Disorders
CWRT: Constant Work Rate Cycle Test
DD: Diaphragm Displacement
DMD: Duchenne Muscular Dystrophy
D-RSBI: Diaphragmatic-Rapid Shallow Breathing Index
ECG: ElectroCardioGram
EPAP: Expiratory Positive Airway Pressure
ERS: European Respiratory Society
ESS: Epworth Sleepiness Scale
FCG: Family CareGiver
FDA: Food and Drug Administration
FEV_1: Forced Expiratory Volume in 1s
FiO_2: Inspired Fraction Of Oxygen
FSHD: FacioScapuloHumeral Dystrophy
FVC: Forced Vital Capacity
GMDN: Global Medical Device Nomenclature
GMED: Groupement pour l'évaluation des dispositifs médicaux
GSPR: General Safety and Performances Requirements
HADS: Hospital Anxiety And Depression Scale
HAS: Haute Autorité de Santé
HFNC: High-Flow Nasal Cannula
HFOT: High-Flow Oxygen Therapy
HI: Health Index
HI-NIV: High-Intensity NIV
HMSN: Hereditary Motor and Sensory Neuropathy
HMV: Home Mechanical Ventilation
HRQL: Health-Related Quality Of Life
ICU: Intensive Care Unit
IFU: Instructions For Use
IPAP: Inspiratory Positive Airway Pressure
IV: Invasive Ventilation
LTH-NIV: Long-Term Home NIV
LT-NIV: Long-Term NIV
LTOT: Long-Term Oxygen Therapy
MAUDE: Manufacturer and User Facility Device Experience
MCS: Mental Component Summary
MD: Medical Deviation or ice
MDR: Medical Device Regulation
MFDS: Ministry Of Food And Drug Safety (South Korea)
MHLW: Ministry of Health, Labour and Welfare (Japan)
MHRA: Medicines and Healthcare products Regulatory Agency (UK)
MPV: Mouth Piece Ventilation
MRC: Medical Research Council scale
MRF26/28: Maugeri Respiratory Failure questionnaire
MS: Multiple Sclerosis
MV: Mechanical Ventilation
MD: Myotonic Dystrophy
NICE: National Institute for Health and Care Excellence
NICE: National Institute for Health and Care Excellence
NIPPV: Non-Invasive Positive Pressure Ventilation
NIV: Non-Invasive Ventilation
NMD: NeuroMuscular Disorder
OHS: Obesity Hypoventilation Syndrome
OSA: Obstructive Sleep Apnoea
PAC: Pressure Assisted/ Controlled

$PaCO_2$: Partial pressure of carbon dioxide in arterial blood
PC: Pectus carinatum
PCO_2: Partial Pressure Of Carbon Dioxide
PCS: Physical Component Summary
PCV: Pressure-Controlled Ventilation
PE: Pectus Excavatum
PEEP: Positive End Expiratory Pressure
PE_{max}: Maximal Expiratory Pressure
PFT: Pulmonary Function Test
PICO: Patient Intervention Comparison Outcome
PI_{max}: Maximal Inspiratory Pressure
PMCF : Post Market Clinical Follow-up
PMS: Post-Market Surveillance
PPV: Positive Pressure Ventilation
PSG: PolySomnoGraphy
PSMA: Progressive Spinal Muscular Atrophy
PSUR: Periodic Safety Update Reports
PSV: Pressure Support Ventilation
PSV-VT: Pressure Support Ventilation Volume regulated
$PtCO_2$: Transcutaneous carbon dioxide
PVA: Patient-Ventilator Asynchrony
QoL: Quality of Life
RCT: Randomised Controlled Trial
RR: Respiratory Rate or Relative Risk
RRxg: generic Residual Risks
RTD: Restrictive Thoracic Disorders
SF-36: Short-Form health survey
SGRQ: St George's Respiratory Questionnaire
SIP: Sickness Impact Profile
SMA: Spinal Muscular Atrophy
SOC: Sense of Coherence Scale
SOFA: Sequential Organ Failure Assessment
SOP: Standard Operating Procedure
SPO_2: Peripheral oxygen saturation
SRI: Severity Respiratory Insufficiency
S(T): Spontaneous Timed
SWT: Shuttle Walk Test
Te: Expiratory Time
TF: Diaphragm Thickening Fraction
TFDA: Taiwan Food and Drug Administration
$Thick_{exp}$: Diaphragm Thickness diaphragm thickness at end-expiration
$Thick_{insp}$: Diaphragm Thickness at end-inspiration
TLC: Total Lung Capacity
TPLC: Total Product Life Cycle
VAPS: Volume-Assured Pressure Support
VAS: Visual Analogue Scale
VCV: Volume-Controlled Ventilation
VE: Minute Volume
V_T: Tidal Volume
VTE : Exhalation tidal volume
VTI : Inspiratory tidal volume
VTS: Volume Target Spontaneous
WACC: Weighted Average Cost of Capital
WHO: World Health Organisation
WMD: Weighted Mean Difference

TABLES

FIGURES

STAGE 0 – SCOPE OF THE CLINICAL EVALUATION

2 SECTION A: NOTIFIED BODY, MANUFACTURER, PRODUCT, CLINICAL EVALUATION REPORT REFERENCE AND TYPE OF EVALUATION

2.1 INTRODUCTION

This CER is a dynamic document based on the analysis of available data on **EO-150 ventilator** produced by EOVE.

As described in the clinical evaluation SOP, a 2-year update was decided for the CER to update, at least, the State of the Art and to review vigilance databases.
This document has to be revised and updated:

- If the manufacturer receives new information from PMS that has the potential to change the current evaluation;
- In case of a significant modification to the product;
  In case of a significant modification to the user or patient information.

The objectives of the clinical evaluation are:

- to establish conformity of the **EO-150 ventilator** with MDR 2017/745 GSPRs and requirements of the European guideline MEDDEV 2.7/1 Rev. 4;
- to provide evidence regarding the intended use (to provide ventilatory support for patients with respiratory insufficiency suffering from acute or chronic respiratory failure), safety and performance of the **EO-150 ventilator**;
- to provide evidence that any risks associated with the use of the **EO-150 ventilator** are acceptable when weighed against the benefits to the patient;
- To identify new misuses/off-label uses and side-effects that could occur using the medical device or similar ones in order to confirm the acceptable benefit/risk ratio acceptability during all the life cycle of the devices.

The report is intended to evaluate the potential risks and benefits which may be associated with the use of the **EO-150 ventilator**, an artificial respirator that provides ventilatory support for patients with respiratory insufficiency. The report seeks to demonstrate the intended purpose of these devices and the claims made in relation to their safety and effectiveness. It seeks to demonstrate that the benefits of using **EO-150 ventilator** clearly outweigh any risks. The report therefore assesses whether sufficient data exist to support the performance and safety claims of these devices.

This report is based on the methodologies for conducting clinical evaluations as described in the following guidelines of the MDR 2017/745:

- MEDDEV 2.7 / 1 Rev 4. Clinical evaluation: a guide for manufacturers and notified bodies;
- MDR 2017/745.

This clinical evaluation has been written by Sarah RENAUD, Consultant (EFOR Group) (CV in APPENDIX 1: CV OF WRITER, REVIEWERS AND APPROVER, Declaration of interests in APPENDIX 2: DECLARATION OF INTEREST) and reviewed by Katharina HOEGL, Technical Specialist, EFOR Group) and Charlotte BENOIT, Head of Clinical Department (EFOR Group) (CV in APPENDIX 1: CV OF WRITER, REVIEWERS AND APPROVER, Declaration of interests in APPENDIX 2: DECLARATION OF INTEREST). From EOVE, [Jean LE ROUX and Cédric JOURDAIN], reviewed the CER and [Patrick DEHOUR], approved it.

2.2 MANUFACTURER

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The person responsible for EOVE's Regulatory Compliance is Patrick DEHOUR. The SRN is FR-MF-000002877

2.3 IDENTIFICATION OF THE DEVICE

2.3.1 List of concerned devices

The following table highlights:
- The concerned medical device: **EO-150 ventilator**
- References of the devices:

Table 1: Devices references

Device	Reference
Main components	
EO-150 ventilator	**EO-150VNT**
EO-150 ventilator module	**EO-VM150**
EO-1X0 Docking station	**EO-DCK1SLT**
EO Charger module	**EO-PWRCHRG**
EO150 Double branch adaptor (interface + expiratory valve)	**EO-DB2-1P-KIT (EO-DB2-1P + EO-DB2-1P)**
Leak and Mouth Piece Adaptor	**EO-LMPADAPT**
Low Flow Connector	**EO-O2CON**
Transport bag	**EO-CARBAG1X0**
Accessories	
FIO2 Cable	**O2CELCBL**
SPO_2 Cable	**EO-SPO2CBL**
Proximal Flow sensor	**EO-PFLOWS**
Remote Alarm Cable 2 m	**EO-ALARMCBL**
Remote Alarm Cable 4 m	**EO-ALARMCBL4**
Upright Bracket	**EO-UPRIGHT**
Roll stand (chariot)	**EO-TROLLEY**
Nomad Bag (no docking station)	**EO-NOMADBAG-EVO**
Travel Bag	**EO-TRVELBAG1X0**
EO-BAT9 Battery pack	
EO-BAT9 Battery Pack	**EO-BATPCK**
Y cable	**EO-CPLPACK**
AC Power/Charger for Y cable	**EO-YCBLPWR**
Commercial variants *	

MV-150 *(variant of the EO-150 ventilator)*	**MV-150VNT**
VEMO 150 *(variant of the EO-150 ventilator)*	**EO-150VEMO**

** These are commercial variants of the EO-150 ventilator and are equivalent in every way other than the name (same technical specifications, IFU etc.).* ***Hence, in this document and all other relative files, the term "EO-150 ventilator" refers to the references EO-150VNT, EO-150VEMO and MV-150VNT.***

*Figure 1: EOVE **EO-150 ventilator***

2.3.2 Device group and Applicable code(s)

The GMDN code associated with the medical device **EO-150 ventilator** is: **47 083** categorised as "Portable electric ventilator".

The CND code associated with the medical device **EO-150 ventilator** is: **Z 120 30 103** categorised as "Extra Hospital Portable Ventilators".

The basic UDI-DI code associated with the medical device **EO-150 ventilator** and its variants are specified in the table below:

*Figure 2: Basic UDI-DI code of the **EO-150 ventilator** and its variants*

Basic UDI-DI	Denomination of the medical device	UDI-DI
376033719EO1503V	EO-150 Ventilator	03760337190054
	VEMO 150 (variant of the EO-150 ventilator)	03760337190047
	MV-150 (variant of the EO-150 ventilator)	03760337190030

2.3.3 Lifecycle

☐ The devices are currently being developed
☐ The devices are presently undergoing initial CE-marking
☒ The devices are CE-marked (since 2015)

The medical device does not undergo reprocessing. The life cycle goes as follows: design, manufacture, use, maintenance, disposal.

2.3.4 Type of conformity assessment

Conformity assessments for the medical device is performed according to ANNEX IX of MDR 2017/745, see document "**100_615 Rev A** - **Conformité à l'annexe IX du règlement 2017/745 ".**
The requirements of EU regulation 2021/2226 are applied and validated with compliance document "**100_877 Rev A – Conformité au règlement UE 2021/2226**."
Conformity assessments for the medical device is performed according to ANNEX I of MDR 2017/745, see the file "**100_613 rev F - Conformité à l'annexe I du règlement 2017-745**".

3 SECTION B: DEVICE DESCRIPTION, CLASSIFICATION, CLINICAL EVALUATION PLAN, MANUFACTURER'S CLAIM, COMMON SPECIFICATIONS AND HARMONISED STANDARDS APPLIED, EQUIVALENCE AND STATE OF THE ART

The following information is extracted from : "**Dossier technique EO-150 UE 2017_745 Rev I** and "**100_23 revDE : user manual_EO-150"** and describes the **EO-150 ventilator** as well as its commercial variants namely, MV-150 and VEMO150.

In the previous version of the EO-150 ventilator CER, there were inconsistencies between the information materials supplied by the manufacturer, the risk management documentation and the State of the Art**.** New risks were identified in the literature that needed to be addressed in the next update of the risk management report and the IFU:

- conventional ventilation mode:
  - aerophagia,
  - claustrophobia,
  - dyspnoea,
  - ventilator-induced lung injury only for invasive ventilation (including barotrauma and volotrauma),
  - increased secretion,
- c-flow mode:
  - heat-related discomfort,
  - thoraco-cervical discomfort.

These elements were included in section "adverse events"(page 2) of the IFU "**100_23 revDE : user manual_EO-150"**.

3.1 INTENDED PURPOSE

The **EO-150 ventilator** device provides continuous or intermittent ventilation support for adult and paediatric patients weighing at least 3.5kg (8lbs). These patients can be ventilator dependent and non-dependent patients and they can required invasive or non-invasive ventilation.
The **EO-150 ventilator** device is intended to be used in home, institution, hospital, portable and mobility environments (i.e. train, car, airplane, wheelchair).

3.1.1 Medical Indications

EOVE **EO-150 ventilator** is designed to treat patients who require continuous or intermittent ventilation support. It can be used for the following chronic indications: COPD, chronic pneumopathies, neuromuscular disorders (NMDs), chest wall disorders and genetic disorders; but also for acute respiratory failures such as COPD exacerbation, acute respiratory failure caused by COVID-19 infection and OHS.

3.1.2 Patient Population

The **EO-150 ventilator** device provides continuous or intermittent ventilation support for adult and paediatric patients weighing at least 3.5kg (8lbs). These patients can be ventilator dependent and non-dependent patients and they can required invasive or non-invasive ventilation.

3.1.3 Intended User

EOVE **EO-150 ventilator** is designed to be used by:
The non-specialist operators, as defined by the ISO norm 80601-2-72:

- the patient;
- the patient's family;
- the caregivers;

The clinical operators:

- doctors;
- nurse;
- physiotherapist;

The responsible organization operators:

- the installation technician;
- the maintenance technician.

3.1.4 Contraindications

Known contraindications are listed in the instructions for use (IFU) file "**100_23 RevDE : user manual_EO-150"** :

- Severe hypotension especially with decreased intravascular volume;
- Pneumothorax/pneumomediastinum;
- Brain surgery or head trauma;
- Cerebrospinal fluid leakage;
- Dehydration;
- Bullous emphysema.

3.1.5 (Undesirable) side effects

Known side effects are listed in the instructions for use (IFU) file "**100_23 RevDE : user manual_EO-150"** and may include:

- Dry mouth/nose;
- Eye irritation;
- Bloating;
- Gastric distension;
- Skin wound;
- Sinus discomfort;
- Aerophagia;
- Claustrophobia;
- Excessive dyspnoea/ventilation dyspnoea;
- Lung injury (including barotrauma and volotrauma);
- Increased secretions;
- Heat discomfort (only for c-flow mode);
- Thoracic discomfort (only for c-flow mode).

3.1.6 Instructions for use

The Instructions for Use are specified in the file "**100_23 revDE : user manual_EO-150"**.
The operating principles of the device and its mode of action are described in detail in the technical notice "**100_022 Rev. DG**", which is a user manual addressed to technical personnel, and the **EO-150 ventilator** user manual "**100_23 revDE : user manual_EO-150"**.

The operation of the ventilator is based on a closed-loop control system of the turbine speed, on the pressure or flow rate set points. The device has two operating modes, barometric mode (pressure control) or volumetric mode (airflow control). The patient circuit can be single or double branch.

In a single-branch patient circuit configuration:

- During the expiratory phase:
  The expiratory valve of the patient circuit is controlled by the internal expiratory control solenoid valve. The turbine speed is then adjusted according to the set expiratory pressure threshold. The measurement and control of the positive expiratory pressure is based on the measurement of the proximal pressure sensor.
  The measurement of the inspiratory flow allows the detection of the patient's inspiratory efforts and triggers the insufflation phase.

- During the inspiratory phase:
  - Barometric mode:
    In barometric mode, control of the turbine speed is based on the measurement of the proximal pressure sensor. The volume delivered to the patient is measured by the inspiratory flow sensor. Volume safety threshold settings warn the patient of low volume (obstruction) or high volume (leakage), with alarm triggers.

  - Volumetric mode:
    In volumetric mode, turbine speed control is based on the measurement of the internal inspiratory flow sensor. The pressure rise is measured by the proximal pressure sensor. The pressure safety threshold setting warns the patient of low (leak) or high (obstruction) pressure, with alarm triggers.

Note: Air and oxygen are mixed at the turbine outlet. Oxygen dosing is done by external controls (litre flow or oxygen concentrator).

The different operating principles of the **EO-150 ventilator** in a single branch configuration are shown below:

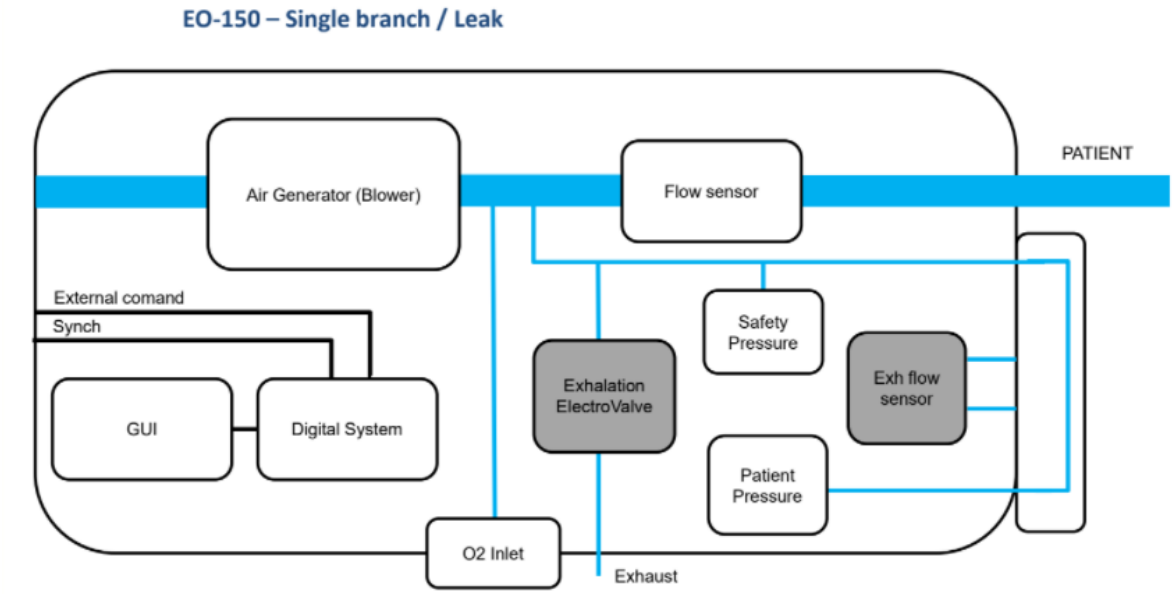


Figure 3: Instruction for use - Single branch / Leak

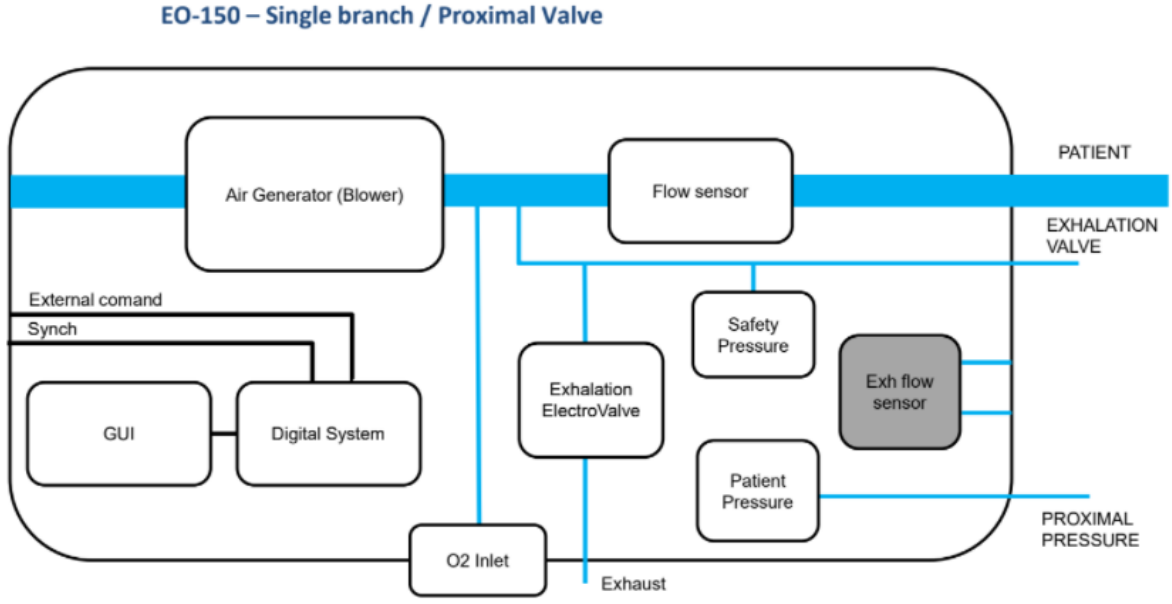


Figure 4: Instruction for use - Single branch / Proximal valve

<u>In a double branch patient circuit configuration:</u>
The operation of the ventilator is identical to the single branch configuration. The only difference is the positioning of the exhalation valve. In the case of a double-branch configuration, the expiratory valve is directly connected to the ventilator (proximal pressure measurement, expiratory flow and expiratory valve control).

The operating principles of the **EO-150 ventilator** in a double branch configuration are shown below:

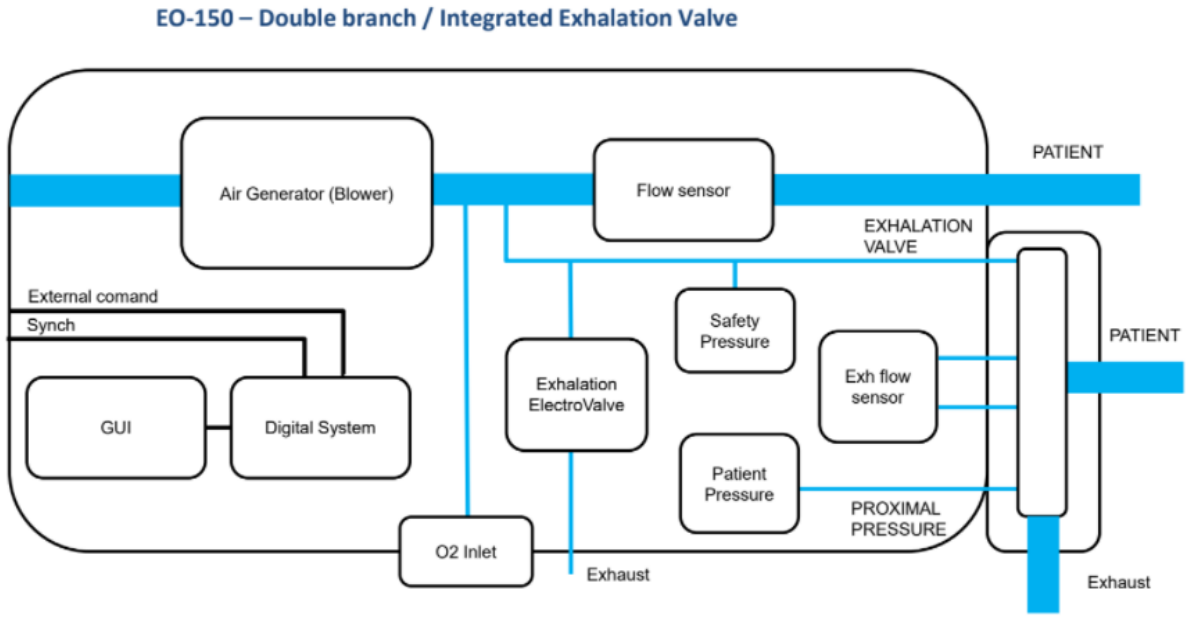


Figure 5: Instruction for use - Double branch / Integrated Exhalation Valve

The **EO-150 ventilator** offers volume or pressure controlled or assisted controlled modes and can be used with the following ventilation modes:

- VAC: Volume Controlled Assisted Ventilation (with expiratory valve)
- VPAC: Pressure Supported Ventilation (with expiratory valve)
- AI: Assisted Inspiratory Ventilation (with expiratory valve)
- MPV: Mouthpiece Volume Ventilation
- MPP: Pressurised mouthpiece ventilation
- AI VR: Volume Controlled Assisted Inspiratory Ventilation (with expiratory valve)
- V-ACI: Volume Intermittent Assisted Ventilation (with expiratory valve)
- P-ACI: Pressure Supported Intermittent Ventilation (with expiratory valve)
- CPAP: Continuous Positive Airway Pressure (with leak)
- ST: Synchronised Spontaneous Ventilation (with leakage)
- PAC: Pressure Supported Ventilation (with leakage)
- VTS: Synchronised Target Volume Ventilation (with leakage)
- C-FLOW: Continuous Flow

3.1.7 Precautions for use and warnings

CAUTION	E0-150 ventilator is not intended for use as an emergency transport ventilator
⚠ **WARNING**	
• **Do not use EO-150 ventilator in an MRI equipment or in a barotherapy equipments.**	
• **A significant risk of reciprocal interference could be posed by proximity of specific investigation or treatment devices.**	

• **The EO-150 ventilator must not be serviced while in use on a patient.**
• **The EO-150 ventilator is not intended for use in oxygen enriched environment.**
• **The EO-150 ventilator is not intended for use with flammable anesthetics and neither for use in conjunction with flammable agents.**

Ventilator dependent patient warnings

WARNING
• **To avoid patient death or serious injury, regularly monitor the patient and ventilator to determine the need to provide emergency ventilation in the event of an audible alarm or ventilator malfunction.**
• **An alternative means of ventilation should always be available for ventilator-dependent patients. Failure to do this may result in patient injury or death. The absence of an alternative means of ventilation such as a second ventilator of the same type or a self-inflating, manual resuscitator (as specified in ISO 10651-4) fitted with a mask may cause the death of the patient in the event of failure of the ventilator.**
• **For a maximum safety, an SPO2 monitor with a low SPO2 alarm activated is recommended for ventilator-dependent patients.**
• **A ventilator dependent patient should always be monitored by trained personnel.**
• **For ventilator dependent patients, in case of failure of the principal ventilator and using a stand-alone ventilation module (without docking station) as a backup device, the backup ventilation module must be used immediately by pressing on the module keypad buttons without inserting it in the docking station of the faulty ventilator. In any case of failure, contact your technical assistance immediately after ensuring the patient is safely ventilated with the backup device and wait for further instructions.**
• **Ensure that the home AC mains supply and connections are safe and comply with the applicable regulations. For ventilator dependent patients, consider using a back-up power system. For safe and adapted solutions, refer to Battery Pack (EO-BAT9) user manual and to the section "Connecting two power sources with Y cable" below.**
• **For ventilator dependent patients in mobility, we strongly recommend not to use internal battery as primary power source. It is mandatory to use an additional power source such as EOVE Battery Pack (EO-BAT9) when the patient is moving away from an external power source (AC or DC).**
• **If a "BAT. CHARGE FAIL" or a "BATTERY FAIL" alarm triggers, the ventilator internal battery needs to be changed. For ventilator dependent patients, contact your technical assistance immediately after ensuring the patient is safely ventilated with the backup device and wait for further instructions.**
• **As the battery ages, the available capacity decreases. When the remaining battery capacity is low, do not rely on the internal battery as the primary power supply and contact your service provider.**
• **When using the EO-150 as a backup ventilator, check and charge the internal battery level regularly (recommended every month).**
• **Some circuit and accessories configurations (mainly in leak pediatric configuration) with high resistive pressure in the circuit could lead to ineffective "Disconnection alarm". For ventilator dependent patient, "Disconnection alarm" must be tested after any calibration, setting changes or circuit configuration change. In case the disconnection alarm detection is not efficient, it is mandatory to set**

a VTI Min alarm (leak configurations) or a VTI Max alarm (valve configurations) as a backup for disconnection events covering.
• **As in CPAP and C-FLOW modes, in a S(T) mode with Rate OFF, the ventilator behaves like a purely spontaneous device (S mode). A patient must have a sufficient ability to breath spontaneously to use this mode. A ventilator-dependent patient cannot be ventilated under such ventilation modes.**

General warnings and cautions

⚠ **WARNING**
Do not cover the ventilator or place it in a position that would alter its proper functioning. **Example 1: Do not place near a curtain so as not to obstruct the circulation of cooling air and thus cause overheating of the ME EQUIPMENT.** • **Example 2: Do not block the air inlet orifice, this could perturbate patient's ventilation.**
• **Do not add intermediate pieces or accessories to the ventilator that are not listed in the operating instructions, otherwise the ventilator may not work properly.**
• **In case of nebulization or humidification, it will be necessary to replace the breathing system filter more frequently to prevent increased resistance or clogging.**
• **When the ventilator is running, use only the travel bag listed in the instructions for use, to avoid any undesirable performance of the ventilator and consequently result in the death of the patient.**
• **To reduce the likelihood of ventilator disconnection and avoid undesirable ventilator performance, use only accessories compatible with the ventilator.**
• **Ventilator accuracy can be degraded by the gas added by the use of a pneumatic nebulizer.**
• **The user and/or the patient must inform its service provider of any serious incident occurred with the device. This information must be notified to EOVE and to competent local authorities if necessary.**
• **Read and understand the entire manual before using the EO-150 ventilator.**
• **The EO-150 ventilator is a restricted medical device intended for use by qualified trained personnel, under the direction of a doctor.**
• **Use the EO-150 ventilator only as directed by a doctor or healthcare provider.**
• **Information in this manual does not supersede instructions given by the prescribing doctor.**
• **Install and configure the EO-150 ventilator in accordance with the instructions given in this guide. Non-specialist operators or institutions encountering problems with set-up, operation or maintenance should immediately contact their EOVE representative.**
• **Verify the effectiveness of ventilation and alarms before connecting a patient to the ventilator.**
• **Handle the EO-150 ventilator and AC power supply with care during and after use especially if ambient temperatures are high as some surfaces may become hot. Do not leave the EO-150 ventilator in direct contact with the patient for extended periods of time.**
• **The EO-150 ventilator should be kept out of reach of children and domestic animals to ensure their safety and the safety of the patient and to avoid damage to the ventilator and the accessories.**
• **The battery and all machine parts of the ventilator and accessories (including trolley) should be disposed of appropriately, following correct regulations for waste management in order to minimize the risk for the environment. They should not be disposed of in household waste.**

• **Ensure that the device and its power charger are placed in a way that allows an easy disconnection from the mains.**
• **Do not use the ventilator at altitude higher than 3000 m, or out of the temperature range 5°C-40°C. Using the ventilator out of these conditions can alter ventilation performance and consequently cause patient death.**
• **Do not supply the ventilator with a wheelchair battery unless this is mentioned in the wheelchair user's instructions or in the ventilator user's instructions, otherwise it could affect ventilator performance and result in patient death.**
• **Ventilator's accuracy can be degraded when using a nebulizer.**

CAUTION
The EO-150 ventilator is not intended for use as an emergency transport ventilator.
Do not expose the EO-150 ventilator to excessive force, do not shake or drop.
If the ventilator or its power supply are dropped or mishandled, immediately discontinue use and contact your EOVE representative.
Repairs and servicing should only be carried out by an authorised EOVE service representative or a qualified and certified service representative.
The airflow for breathing produced by the ventilator can be higher than the temperature of the room by up to 6°C. Exercise caution if the ambient air in the room exceeds 35ºC.

Operation Warning and precaution measures

WARNING
• **Blocking the air inlet could lead to patient injury.**
• **Keep machines clear of blankets, soft toys, and dust. Keep out of direct sunlight.**

CAUTION
To prevent possible damage to the ventilator always place it on a flat, dry and stable surface. To protect the device during transportation, always ensure that the EO-150 ventilator is transported using the EOVE Transport bag, Nomad bag or Travel bag.
Always protect the device from water if used outdoors.

Set Up test

WARNING
• **If alarms do not sound during the Set Up test, do not use the ventilator.**

CAUTION
Contact your healthcare provider or EOVE for assistance if any of the checks in the set up test fail.

If the EO-150 has been returned after servicing, ensure it is clearly labelled as disinfected before starting the set-up test or installing.

To perform Set Up test

• **If any of these steps** [Set up test steps] **fails, do not use the EO 150 ventilator. Contact your healthcare provider or your Eove representative for a device checking.**
• **Some circuit and accessories configurations (mainly in leak pediatric configuration) with high resistive pressure in the circuit could lead to ineffective "Disconnection alarm". For ventilator dependent patient, "Disconnection alarm" must be tested after any calibration, setting changes or circuit configuration change. In case the disconnection alarm detection is not efficient, it is mandatory to set a VTI Min alarm (leak configurations) or a VTI Max alarm (valve configurations) as a backup for disconnection events covering.**
• **The EO-150 ventilator cannot be powered off during ventilation**

Turning off the ventilator

⚠ **WARNING**
• **The EO-150 ventilator cannot be powered off during ventilation**

Navigating the Patient screen and menu

⚠ **WARNING**
• **The sound level should be adjusted according to the criticality of the patient.**

Patient circuit, power supplies and accessories configurations

⚠ **WARNING**
• **Use only CE marked circuit components compatibles for use with the EO 150.**
• **When using a non-invasive interface, the measurement of patient exhaled gas volume may be affected by leaks.**
• **To ensure correct functioning of the circuit, it is recommended that a calibration be performed at the installation of each new circuit.**
• **Install patient circuit tubing carefully, to avoid risk of strangulation or tripping.**
• **The responsible organization must guarantee compatibility of the ventilator with all accessories intended to be used for patient connection before usage.**
CAUTION
For pediatric patients, ensure that the breathing circuit type is suitable for use with a child. Pediatric patient circuits should be used when tidal volume is lower than 300 ml.

Calibration

WARNING
• **Mask with leak can be added at step 5 (open circuit) for more accurate pressure measurements and more efficient disconnection alarm. This should be considered in particular for new-born patients.**
• **Some circuit and accessories configurations (mainly in leak pediatric configuration) with high resistive pressure in the circuit could lead to ineffective "Disconnection alarm". For ventilator dependent patient, "Disconnection alarm" must be tested after any calibration, setting changes or circuit configuration change. In case the disconnection alarm detection is not efficient, it is mandatory to set a VTI Min alarm (leak configurations) or a VTI Max alarm (valve configurations) as a backup for disconnection events covering.**

Double limb circuit with adapter EO-DB2-1P-KIT

CAUTION
The double limb circuit adaptor is single-patient-use and disposable. Only using an expiratory filter and observing its manufacturer recommendations can prevent from cross-contamination and allow its reuse.
WARNING
This accessory is compatible with humidification systems. However, prolonged exposure to condensation can lead to misfunctioning of the VTE measurement. If that happens, removing and blowing the adaptor with air will solve the issue. It is recommended to regularly inspect the adaptor and adapt the humidification system or the humidification level if condensation is noted.

Single limb with intentional leak

WARNING
• **Rebreathing may occur when using a single limb circuit with intentional leak if the pressure is too low for a given leak diameter.**
• **Ensure the vent holes at the mask or constant leaks at the vented interface port are not obstructed.**
• **As far as possible, particularly in pediatric configuration, calibration must be performed with the maximum possible accessories (including mask if necessary) to optimize pressure measurements and disconnection alarm performance. Disconnection alarm must always be tested in the complete configuration after calibration. Low Vti alarm must be used in case of disconnection alarm not efficient.**

Accessories compatible with the EO-150 ventilator

WARNING
• **Before using any accessory, always carefully read the accompanying Quick User Guide and User Manual.**
• **Before using EO-BAT9 Battery Pack (EO-BATPCK), read the accompanying EO-BAT9 User Manual.**

• **The EO-150 Ventilator should only be used with accessories recommended by EOVE. Connection of other accessories could result in patient injury or damage to the device.**

Attaching patient circuit accessories

⚠ **WARNING**
• **Adding or removing circuit components can adversely affect ventilation performance.**
• **A circuit calibration is recommended every time an accessory or component is added to or removed from the patient circuit.**
• **Do not use electrically conductive or anti-static air tubing.**

Attaching an antibacterial filter

⚠ **WARNING**
• **To prevent the risk of cross-contamination, an antibacterial filter is mandatory if the device is to be used on multiple patients.**
• **Regularly check the antibacterial filter and expiratory valve for signs of moisture or other contaminants, particularly during nebulization or humidification. Failure to do so could result in increased breathing system resistance and/or inaccuracies in expired gas measurement.**
• **Only use antibacterial filters that comply with the relevant safety standards, including ISO 23328-1 and ISO 23328-2.**
CAUTION
The antibacterial filter must be used and replaced according to the manufacturer's specifications.

Attaching a humidifier

⚠ **WARNING**
• **Humidification of the inspired gas is required for invasive ventilation in order to prevent any lung injury.**
• **Always place the humidifier on a level surface lower than level of the ventilator and the patient in order to prevent the mask and tubing filling with water.**
• **Ensure that the humidifier is set up according to the manufacturer's instructions.**
• **Use appropriate precautions to prevent water in the circuit transferring to the patient (e.g. a water trap).**
• **Only use HMEs that comply with the relevant safety standards, including ISO 9360-1 and ISO 9360-2.**
CAUTION
Make sure that the water tub is empty and thoroughly dried before transporting the humidifier.

Attaching oxygen

WARNING
• **Use only medical grade oxygen.**
• **Ensure that the device is ventilating before the oxygen supply is turned on.**
• **The oxygen flow must be turned off when the device is not ventilating so that oxygen does not accumulate within the device. The accumulation of oxygen presents a fire risk.**
• **Oxygen supports combustion. Only use oxygen in well-ventilated rooms. Using oxygen while smoking or in the presence of an open flame creates a fire hazard.**
• **Supplemental oxygen must be added into EO 150 ventilator's oxygen inlet at the rear of the device.**
• **Monitor supplemental oxygen using the optional FiO2 cell and relative alarms.**
• **O2 inlet is designed for functioning up to 50 kPa during ventilation, however oxygen sources up to 400 kPa can be used since a flow regulator limits flows below 20 l/min. If O2 pressure rises above 50 kPa when stopping ventilation, there is no risk for the ventilator, but the oxygen source tubing may disconnect from the oxygen adaptor. In this case, the oxygen supply must be cut off immediately.**
• **Connect to the ventilator inlet adaptor, always flexible tubing without additional fastening means. Never use a collar or anything to increase tubing resistance to pressure at ventilator inlet, this could result in damaging the ventilator.**
• **Always turn off the oxygen supply when ventilation is stopped for any reason.**
• **The EO-150 ventilator is not designed for use with anesthetic gases.**
• **Oxygen can be added up to a maximum flow of 20 l/min. Considering this limitation, it is not always possible to reach Fi02 concentrations above 50%. In C-Flow mode, O2 Flow can be increased up to 60 l/min to reach higher concentrations, however the O2 flow must stay below the set flow to avoid any risk.**
• **For a given O2 flow, O2 concentration may vary with many parameters such as volume, inspiratory time, rate, PEEP, leak, interface, patient circuit.**

Attaching a FiO_2 sensor

WARNING
• **The EO-150 ventilator can be used with an optional FiO2 sensor with minimum and maximum concentration alarms. This sensor should always be used to ensure that the prescribed oxygen concentration is delivered to the patient.**
CAUTION
To display the FiO2 measurements and to set the alarms, activate FiO2 monitoring in the configuration menu. When activating the sensor, it will perform a calibration at ambient 21%. The sensor needs to be free from O2 for this calibration.

T piece and cell installation

⚠	**WARNING**
•	**Measurement is influenced by the O2 cell position. FIO2 cell must be placed vertically to have expected measurement performance.**

Attaching a pulse oximeter

⚠	**WARNING**
•	**Only use compatible NONIN finger pulse sensors**
	CAUTION
	Some factors may degrade the performance of the pulse oximeter or affect the accuracy of the readings (e.g. blood flow restrictors, arterial catheters, blood pressure cuffs, infusing lines, etc.), excessive ambient light, excessive motion, electromagnetic interference, moisture in the sensor, improperly applied sensor, incorrect sensor type, a sensor not at heart level, poor pulse quality, venous pulsations, anemia or low hemoglobin concentrations, cardiogreen or other intravascular dyes, carboxyhemoglobin, methemoglobin, dysfunctional hemoglobin, artificial nails or fingernail polish.
	To remove the cable, pull firmly on the locking ring. Do not twist.
	If used in conjunction with the Sentec monitor, the SPO2 and Heart rate signal will be taken from the NONIN sensor.

Power connections

⚠	**WARNING**
•	**Beware of electrocution. Do not immerse the device, power supply or power cord in water.**
•	**Make sure the power cord and plug are not damaged and the equipment is in good condition.**
•	**Keep the power cord and device away from hot surfaces.**
•	**Explosion hazard—do not use in the vicinity of flammable anesthetics.**
•	**Ensure that the device and its power charger are placed in a way that allows an easy disconnection from the mains.**

Connecting to main power

⚠	**WARNING**
•	**Ensure that the power cord does not pose a tripping or choking hazard.**
•	**Ensure that the home AC mains supply and connections are safe and comply with the applicable regulations. For ventilator dependent patients, consider using a back-up power system. For safe and**

	adapted solutions, refer to Battery Pack (EOBAT9) user manual and to the section "Connecting two power sources with Y cable" below.
NOTE	Do not twist or tug the power cord or the outer housing of the connector.

Running the ventilator on internal battery

⚠	**WARNING**
•	**When using the EO-150 as a backup ventilator, check and charge the internal battery level regularly (recommended every month).**
•	**As the battery ages, the available capacity decreases. When the remaining battery capacity is low, do not rely on the internal battery as the primary power supply and contact your service provider.**
•	**For ventilator dependent patients in mobility, we strongly recommend not to use internal battery as primary power source. It is mandatory to use an additional power source such as EOVE Battery Pack (EO-BAT9) when the patient is moving away from an external power source (AC or DC).**
•	**The internal battery should be replaced every two years, or when a service notification is displayed.**
•	**Replacement of lithium batteries or fuel cells by anyone other than trained personnel will result in dangerous risk (e.g., excessive temperatures, fire or explosion)**
•	**The internal battery and any other device component should be disposed of following appropriate waste management regulations.**
	CAUTION
	Plug device into AC mains power when the remaining capacity of the battery is low.
	The internal battery may stop charging when ambient temperatures of 35°C or more are reached.
	If AC power is lost, the battery is guaranteed to continue to provide ventilation for a limited duration. Find an alternate supply or alternative means of ventilation e.g. back-up ventilator or manual ventilation means.
	If the EOVE device is left in storage for an extended period of time the internal battery will become depleted. If storing your device, recharge the internal battery once every six months. Never store a device with an empty battery.
	Storing the ventilator at temperatures higher than 50°C for extended periods will accelerate battery ageing. This will not affect the safety of the battery or the device.

Battery run time

⚠	**WARNING**
•	**Those reference internal battery run time are given for a ventilation module without docking station. When used with docking station, the resulting operation time will depend on luminosity setting and stand-by mode option and can be reduced by 20% to 30%. Always look at the device indication to know the real conditions expected autonomy.**

Connecting to an external DC power source

⚠	**WARNING**

• **When using a car auxiliary adapter, start the car before plugging in the DC Adapter of the device and unplug the ventilator before stopping the car. The car start/stop functionality must be deactivated.**
• **If the external DC power source drops to below 12V, the EO-150 ventilator will switch to internal battery.**

Connecting a Y cable with Battery Pack (EO-BAT9) and AC Power/Charger (EO-YCBLPWR)

⚠	**WARNING**
•	**When using the Y cable solution with (EO-BAT9) and AC Power/Charger (EO-YCBLPWR). The Battery Pack (EO-BAT9) needs to be charged at least every two weeks with its own charger. Regularly check the Battery Pack autonomy level indicated on the Battery Pack keypad.**
	CAUTION
	The shorter part of the Y cable needs to be connected to the primary power source (AC Power/Charger)
NOTE	In case of AC power loss combined with a battery failure while using the Y cable solution with (EO-BAT9) and AC Power/Charger (EO-YCBLPWR), the ventilator can reset and restart ventilation normally within 5 seconds.

Mounting EO150 on trolley (EO-TROLLEY)

⚠	**WARNING**
•	**When using the trolley in combination with EO150 and other accessories, always verify a maximum weight of 20 kg is not exceeded. Always use the handle to move the trolley (always pull, do not push). Not respecting this could result in damaging the ventilator or causing patient injury.**
•	**Use only screws delivered by Eove. Otherwise, there is a risk to damage the ventilator or its accessories.**
	CAUTION
	Make sure to push the upright brackets until the contact with the lower housing to ensure good support for the device
	Be sure to check the positioning of the upright brackets after moving the device

Travelling with EO150 ventilator, the Click-and-Go system

⚠	**WARNING**
•	**The EO-150 ventilator should not be operated while in the Transport bag. To ventilate while travelling, use the EO-Series Ventilator accessory bags: Nomad bag or Travel bag.**
•	**For ventilator dependent patients in mobility, we recommend the usage of an additional power source such as Battery Pack (EO-BAT9).**
	CAUTION
	Do not place any heavy or bulky objects in the zippered pocket on the inside front of the bag. This could result in damage to the touch screen.

Using the Transport bag

⚠	**WARNING**
•	**The Transport bag is only to be used to transport the ventilator. Ventilation cannot take place when the ventilator is in this bag.**

Alarms

⚠	**WARNING**
•	**Test the effectiveness of the alarm after any changes to the circuit, ventilation settings or co-therapy. Alarm settings are sensitive to these changes.**
•	**Alarms may deactivate if the alarms are set to extreme values. This could put the patient at risk.**

Routine cleaning and maintenance

⚠	**WARNING**
•	**The EO-150 ventilator must not be serviced while in use on a patient**
•	**Ventilation dependent patients are vulnerable to infections. All equipment should be regularly cleaned and disinfected.**
•	**Keep the device, and accessories away from water. Always turn off and unplug the device before cleaning and verify that it is dry before plugging it back in.**
	CAUTION
	Clean only exterior surfaces of the EO150 Ventilator device.
	If necessary, wipe the exterior of the device with a damp cloth using a mild cleaning solution.
	For all circuit components and hoses, follow the manufacturer's recommendations for cleaning and maintenance.
	The air filter cannot be washed or reused.

Servicing

⚠	**WARNING**
•	**Maintenance of the ventilator should be carried out by a trained technician. Attempting to repair the machine yourself could result in patient injury or damage to the machine.**
•	**It is forbidden to modify the EO 150 without manufacturer authorization.**
NOTE	Retain the original packaging to use when shipping to/from service agent.

Device information : Technical specifications

WARNING
• **Due to their resistance to flow, accessories such as filters, water traps and humidifiers many decrease patient pressure during inspiration and increase patient pressure during exhalation.**

WARNING
• **The C-Flow mode cannot be considered as a ventilation mode since it is not providing pressure and flow directly to the patient.**
• **As in CPAP and CFLOW modes, in a S(T) mode with Rate OFF, the ventilator behaves like a purely spontaneous device (S mode). A patient must have a sufficient ability to breath spontaneously to use this mode. A ventilator-dependent patient cannot be ventilated under such ventilation modes.**
CAUTION
In Spontaneous mode (S(T) mode with Rate deactivated), the disconnection alarm will trigger if an apnea is longer than the Disconnection alarm timer is set. To avoid annoying alarms, the disconnection timer needs to be set at a higher value than the maximum expected apnea times.

Alarm parameter specifications

WARNING
Delaying or deactivating the disconnection alarm through the disconnection timer must be done only with patients that have the corresponding capacity of breathing spontaneously. Failure to apply this recommendation can lead to a life-threatening risk for the patient.

Power specifications

WARNING
• **This device is intended to function with external power supply 2440 from Mascot, never use any other power supply unless recommended by Eove.**
• **To disconnect the device from the mains, unplug power supply.**

Guidance and manufacturer's declaration electromagnetic emissions & immunity

WARNING
• **The ventilator should not be used in close proximity to other equipment or stacked on top of other devices. If this kind of use is unavoidable, the ventilator should be checked carefully and observed to ensure correct functioning of the device.**
• **Only accessories recommended for the EO 150 should be used. Using any other accessories could result in risk to the device or the patient.**

• **Any additional equipment connected to medical electrical devices must comply with the respective IEC or ISO standards (e.g., IEC 60950 for data processing equipment).** • **Furthermore, all configurations shall comply with the requirements for medical electrical systems (see IEC 60601-1-1 or clause 16 of the 3Ed. of IEC 60601-1, respectively). Adding additional equipment configures a medical system and this system must comply with the requirements for medical electrical systems. Any person undertaking this kind of addition shall be responsible to ensure that all requirements are complied with. It is important to note that local laws take priority over the above-mentioned requirements. If in doubt, consult an EOVE representative or the technical service department.**
• **Interference may occur in the vicinity of equipment marked with the following symbol:** 
• **EO150 is designed for use in the electromagnetic environment described below. Those using the device should ensure that the EO 150 is used in such an environment.**

3.1.8 Storage conditions

During a storage period or a long period of non-use, the docking station should be switched off.

If the EOVE device is left in storage for an extended period of time the internal battery will become depleted. If the device is being stored, recharge the internal battery once every six months. Never store a device with an empty battery.

Prepare the battery for long-term storage:

1. The battery charge level should be 100%.
2. Turn off the device.
3. Remove the power cord from the device.

As per the information found on the packaging, the **EO-150 ventilator** must be stored upright and kept dry. Additionally, ambient temperature for storage should be from -20°C to +60°C and relative humidity from 10% to 95%, (non-condensing).

3.1.9 Lifetime of the device

There is no expiry date.

The medical device does not undergo reprocessing. The life cycle goes as follows: design, manufacture, use, maintenance, disposal.

According to the file "**100_616_B_lifetime evaluationEO150**" the lifespan of the device of is 10 years; provided that the IFU and maintenance schedule are correctly followed (average use of 16 hours per day). This expected shelf life is valid for all the following **EO-150 ventilator** components: electro valve, flow sensor, CPU board, keyboard, AC connector, piston board connector, and the GIU tactile interface. The manufacturer's indicated shelf life is in line with maintenance recommendations.

*Table 2: **EO-150 ventilator** components shelf life information*

Component	Manufacturer shelf life indication	Associated maintenance measures	Expected use in maintenance time (10 years if no maintenance)	Manufacturer shelf life in line with maintenance recommendation ? (Yes/No)
Motor turbine MFA0300 I Ref.: 200A0106 / 200A0106	> 40 000 hours (See attachment 3)	Replacement after 20 000/30 000 hours for paediatric/adult use	20 000/30 000 hours for paediatric/adult use	Yes
Electro valve Ref.: Preciflow LS202A515 24VDDC	MTBF > 100 millions cycles	Replacement after 100 millions cycles	100 millions cycles	Yes
Sensor flow Ref.: SFM3000-200-C	10 years (See attachment 1 for rational)	4 years	24 000 hours	Yes
CPU Board Ref.: CPU Board EO151	Internal development. MTBF test in attachment 2: Result = 80 000 hours	NA	58 400 hours	Yes
Keyboard Ref.: 544030 ENS C	Buttons: 500 000 pushes LEDs: 73 300 hours (See attachment 4)	NA	Buttons: 73 000 pushes LEDs: 58 400 hours	Yes
AC Connector Ref.: L722RAS	10 000 cycles connection/disconnection (See attachment 5)	NA	7 300 cycles	Yes
Piston board connector Ref.: 811-S1-002-10-017101	50 000 cycles connection/disconnection (See piston technical sheet - attachment 6)	NA	7 300 cycles	Yes
GUI Tactile interface Ref.: UMOH-9597MD-1T	1 467 812 hours (see calculation note in attachment 7)	NA	58 400 hours	Yes

3.2 DEVICE DESCRIPTION

3.2.1 Device technical description

3.2.1.1 Main materials

As a preamble to the choice of materials, the **EO-150 ventilator** is not an implantable device and is not in direct contact with the patient. Tubing and masks or cannulas are not supplied with the device and are purchased separately by users from other manufacturers.

The external battery (EO-BAT9 battery pack) is developed by EOVE and allows the **EO-150 ventilator** to be powered on the move. Details are given in the product manuals and it is the subject of a separate evaluation report (CER "**101_74 revB - CER_EO-BAT9**" and technical File "**Dossier technique EO-BAT9 UE 2017_745 Rev D**").

During the design, the materials composing the air pathway were selected among plastic and materials approved for food usage, or in conformity to the ISO 10993 standard, based on the material datasheet and/or certificate given by the supplier.
In the table hereafter are listed the level of compatibility reached by the different materials composing the air pathway:

*Table 3: Materials of **EO-150 ventilator** components of the air pathway*

Component	Material	Level of biocompatibility
Air inlet filter cover	Terluran GP-22 (ABS)	FDA and CE Food contact grade
Output to patient insufflation	Terluran GP-22 (ABS)	FDA and CE Food contact grade
Blower - volute/carter plastic	PC MAKROLON 2458	ISO 10993 and USP class VI
Blower – blae	PEEK 450 G Natural	EN 10204 - FDA Food contact grade
Turbine foam	REGISEAL TN 30 FR	NA
Blower - silicone part	SILPURAN 4200	ISO 10993 and USP class VI
Flow sensor	PPE+PS	ISO 10993 and USP class VI
Air inlet filter foam	JBM PPI 75	NA
Patient outlet foam	JBM PPI 30	NA

*Note: The material certificates are recorded in "***100_79 H Raw materials & critical components list"**

There are no components with a substances concentration higher than 0.1%. Further details are provided in the biocompatibility report issued for the device (see section 12).

The table below lists raw materials of some components used in **EO-150 ventilator**. These raw materials are classified into 4 categories :

- Materials of Mains Components (AC voltage)
- Materials of High reliability Components
- Materials in contact with the air insufflated to the patient
- Materials compliance with UL 94 (the standard for the flammability safety of plastics)

*Table 4: Raw materials of the **EO-150 ventilator** main components, high reliability components, those in contact with the air insufflated to the patient and materials compliant with UL94 standard*

Designation of components	Reference of material used for components	Manufacturer of components	Supplier of article using these components	Norm & Standard	Reference of annexed document
Mains Components (AC voltage)					
Mains Cord Europe	XVI-H03VVH2F2x0,75-C7/1,5m	FELLER	NA	VDE	2S
AC/DC Power supply	2440 PSU 24V	MASCOT	NA	IEC 60601-1	5S
High reliability Components					
Motor Turbine MFA300	200A0106	Electromag	AIRFAN (turbine)	NA	1HF
Motor Turbine MFA290	200A0138A	Electromag		NA	1HF bis
Lion battery cell	Li Ion Samsung cells INR18650-30Q (2950 mAh).	SAMSUNG SDI Co., Ltd.	VLAD (Battery)	NA	2HF bis
Electro-valve Proport.	Preciflow LS202A515 24VDC	ASCO	NA	NA	3HF
Sensor flow	SFM3000-200-C	SENSIRION	NA	NA	5HF

Materials in contact with the air insufflated to the patient					
Insufflation port part	M08068B26-colorant blanc Terluran GP-22 (ABS)	Elian STYROLUTION	OCCITANIE PLASTIQUE	FDA, CE compliant	1MPbis
Air input part	Terluran GP-22 (ABS)	STYROLUTION		FDA, CE compliant	1MPbis
Turbine impeller	PEEK 450 G Natural	VITREX	AIRFAN (turbine)	EN 10204	2MP
Turbine volute	PC MAKROLON 2458	BAYER		ISO10993	3MP
Turbine casing	PC MAKROLON 2458 (MEVOPUR 3%)	BAYER		ISO10993	4MP
Turbine foam	REGISEAL TN 30 FR	FOAM PARTNER		NA	5MP
Turbine silicon part	SILPURAN 4200	WACKER		ISO10993	6MP
Air inlet filter foam	JBM PPI 75	TECMATEL	TECMATEL	ISO 845 / ISO 3386/1 ISO 1798	11MP
Turbine output foam	JBM PPI 30	TECMATEL		ISO 845 / ISO 3386/1 ISO 1798	12 MP
Material UL94V0					
Enclosure – Housing	Luran S KR 2867 C WU	STYROLUTION	OCCITANIE PLASTIQUE	UL94V0	1MFbis
PCB – CPU board	Voir fiches E229342 / E207844	SUNSHINE GLOBAL CIRCUITS / SUNTAK MULTILAYE R PCB	INOVELEC (CPU Card)	UL94V0	4MF et 4MF bis
PCB - Station Eo-display	Voir fiches E154554 / E357349	KUNSHAN SUHANG CIRCUIT BOARD / SAFE		UL94V0	5MF et 5MF bis

This table below lists some of critical components of the **EO-150 ventilator** according the IEC standards.

*Table 5: Table of **EO-150 ventilator** critical components according to IEC standards*

Component/ Part No.	Manufacturer/ Trademark	Type No./model No./	Technical data	Standard No./, Edition	Mark(s) & Certificates of conformity1)
Power supply	MASCOT	Type 2440	100-240VAC 50-60Hz 1,6A Output 28VDC ; 2,5A Class II PS ; IP41	IEC 60601-1	cURus E356182
European Power supply cord	FELLER	XVIH05VVH2F2 X075-C7W/1,80M SW9005 L37	Plug type XVI, 2,5A 250V	EN50075	ENEC 11
			Cord type H05VVH2F2X0, 0,75mm²	EN 50525:2011 EN 50525-2-11:2011 EN 50395:2005 + A1:2011 EN 50396:2005 + A1:2011	HAR, OVE
			Connector Type C7W 2,5A 250V	EN60320-1:2015 UL817 C22.2 No.21, JIS C8303	ENEC 11

US CA power cord	FELLER	Plug NEMA 1-15 Cord SVT2X18AWG Connector C7W	1,80m, black 7A/125V AC	UL 62 IEC 60320	UL, CSA
JP power cord	FELLER	Plug N1/15J Cord VCTFK 2x0,75 Connector C7	2,5m, black 7A/125V AC	JIS C 8303 JISC 3306	PSE (JET)
EO-150 Ventilator module, REF EO-VM150					
Plastic enclosure	ALBIS PLASTIC GMBH	KR2867 CWU	Acrylonitrile Styrene Acrylate/Polycarbonate (ASA/PC) V-0 for 1,5mm	IEC 60695-11-10 UL 94	cURus E80168
Wiring	ALPHA WIRE CO	2842/7	PTFE insulation 28AWG VW-1 ; 80°C	UL 758	UR E163869
Connectors	JAPAN SOLDERLE SS TERMINAL MFG CO LTD	B6B-ZR-SM4-TF	V-0	UL 1977	UL E60389
Connectors	MOLEX	53398 series 53398-0871 53398-0471 548190572 22122104 - 7478 526101033 53398-0671 436500326 22-23-2041 - 6373	V-0	UL 1977	UR E29179
Connectors	SAMTEC INC	TFM-107-01-S-DRA SFM-107-02-S-D TFM-107-01-S-DRA TFM-107-02-S-D	V-0	UL 1977	UR E111594
+ PCB	SUNSHINE GLOBAL CIRCUITS CO LTD	All types	V-0	UL 94 UL 796	UR E229342
	SUNTAK MULTILAYER PCB CO LTD	SMT-5	V-0 ; 130°C	UL 94 UL 796	cURus E207844
Battery Li-ion	VLAD	EOVE 3 –6INR19/66 6S1P Li-Ion	Li-ion : 21,6V – 2.95Ah – 63.7 Wh Cells SAMSUNG INR18650-30Q	IEC 62133-2	LCIE Test report 166234-748670 B
Primary battery	PANASONIC	CR1220	3V Max abnormal charging current	UL 1642	UR MH12210

			3mA		
Motor	ELECTROM AG	200A0138A	24 Vdc, 4,8 W	IEC 60601-1	Tested in this test report
Docking Station EO-AX0, REF EO-DCK1SLT					
Plastic enclosure	ALBIS PLASTIC GMBH	KR2867 CWU	Acrylonitrile Styrene Acrylate/Polycarbonate (ASA/PC) V-0 for 1,5mm	IEC 60695-11-10 UL 94	cURus E80168
+ Main board PCB	KUNSHAN SUHANG CIRCUIT BOARD CO LTD	SH-M1	V-0 ; 105°C min	UL 94 UL 796	UR E154554
+ wifi board	KUNSHAN SUHANG CIRCUIT BOARD CO LTD	All types	V-0 ; 105°C min	UL 94 UL 796	UR E154554
	SAFE COMPANY LTD	SAFE-4	V-0, 130°C	UL 94 UL 796	cURus E357349
Primary battery	PANASONIC	CR1220	3V Max abnormal charging current 3mA	UL 1642	UR MH12210
Electric fan	SUNONWEALTH ELECTRIC MACHINE INDUSTRY CO LTD	MC35100V2	DC5V 0,38W	UL 507	cURus E77551
Connectors	HIROSE ELECTRIC CO., LTD.	HIROSEDF63SF_3PTS	V-0	UL 1977	UR E52653
Connectors	SAMTEC INC	SAMTEC_BTH-70P	V-0	UL 1977	UR E111594
Connectors	TE CONNECTIVITY INDUSTRIAL GMBH	M.2_PCI.E	V-0	UL 1977	UR E247738
Connectors	JAPAN SOLDERLESS TERMINAL MFG CO LTD	NSH series	V-0	UL 1977	UL E60389
Connectors	WUERTH ELEKTRONIK EISOS GMBH & CO. KG	USB_MICRO-AB-5	V-0	UL 1977	UR E323964

Connectors	AMPHENOL LTW TECHNOLOGY CO LTD	EMBA_000014_A 87520-0010BLF	V-0	UL 758	UR E489039

3.2.1.2 Main physical and mechanical characteristics

The general system:

The general ventilation system is composed of:

- A docking station, which allows the installation of ventilation blocks, and which will have a graphic system (touch screen graphic display + advanced operating system) for the user interface,
- A slot allowing the insertion of a ventilation module,
- A ventilation unit ensuring the ventilation and safety functions except for the display.

The docking station is composed of:

- 1 slot for the reception of a ventilation module,
- 1 place for the positioning of a name or brand,
- 1 physical grip (handle) for lifting and carrying the unit,
- 1 electronic board defining the graphic system and its associated operating system for the user interface function and the connection with the ventilation blocks,
- 1 7'' multi-touch graphic display.

The ventilation unit:

The extractable ventilation unit consists essentially of the following elements:

- 1 micro-turbine,
- 1 electronic board composed of all the ventilation intelligence,
- 1 flow sensor,
- 1 exhalation pilot valve,
- 1 oxygen inlet shut-off valve,
- 1 membrane keyboard,
- 1 Li-ion battery,
- 1 DC power connector,
- 1 electrical connector for inter-block communication,
- 1 pneumatic connector 22mm for connection to the patient,
- 4 pneumatic connectors for connection to various sensors and exhalation valves,
- 1 air inlet filter,
- 1 pneumatic connection for the connection of a low pressure oxygen source.

The **pneumatic block** of the ventilation module offers the following pneumatic connections:

- 1 pneumatic connector male ∅ 22mm for connection to the patient,
- 2 male pneumatic connectors for the pneumatic connection of a proximal flow sensor,
- 1 pneumatic male connector for the pneumatic connection of the proximal pressure sensor,
- 1 pneumatic male connector for the connection of the exhalation valve control.

The ventilation module integrates the following electrical or wireless connection possibilities:

Wireless connection:

- 1 Bluetooth connection to allow communication with the external remote control element (start/stop ventilation, boost, monitoring, etc...) accessible via Smartphone, tablet, etc...

Wired connection:

- 1 DC power connector,
- 1 FiO_2 sensor connector,
- 1 normally open or normally closed alarm reminder connector,
- 1 USB Host (µUSB) connector for communication with the block (programming, data consultation) - backup/debugging connection. This connector will not be accessible from the outside,
- 1 electrical connector for communication with the interface of the docking station.

The following figures show the **EO-150 ventilator** (front and rear views) and clearly indicates its features.
Figure 6 shows a front view of the **EO-150 ventilator** in which the display screen, ventilation module, Proximal pressure, valve, and proximal flow connectors, housing unit, inspiratory/circuit port and menu bar/keyboard are clearly displayed.

*Figure 6: Front view of the **EO-150 ventilator** and description of its features*

1. Display screen	4. EO device housing unit
2. Ventilation module	5. Inspiratory / Circuit Port
3. Proximal pressure, valve, and proximal flow connectors	6. Menu bar / keyboard

Figure 7 shows a rear view of the **EO-150 ventilator** in which the Air inlet and hypoallergenic filter, DC power connector, docking station power button, USB-1/2 ports, O2 input, FiO2/peripheral oxygen saturation (SpO_2) connector and remote alarm connect are clearly displayed.

*Figure 7: Rear view of the **EO-150 ventilator** and description of its features*

1. Air inlet and hypoallergenic filter	5. USB-1 port (data retrieval)
2. DC Power connector	6. O_2 input
3. Docking station Power Button	7. FiO_2 / SpO_2 connector
4. USB-2 port (maintenance only)	8. Remote Alarm connector

Figure 8 shows a rear view of the **EO-150 ventilator** without housing in which the USB port, DC car charger and outer housing connections are clearly displayed.

*Figure 8: Rear view of the **EO-150 ventilator** without outer housing and description of its features*

1. USB port (Do not use - limited to maintenance operations as described in the maintenance manual)	3. Connection to outer housing
2. DC Car charger connection	

Menu Bar / Keyboard

Figure 9 shows the keyboard/menu bar of the **EO-150 ventilator** in which all the indicators (power source, high priority alarm, technical alarm, circuit alarm, physiological alarm, medium priority alarm and battery life) and switches (ventilation start/stop, ON/OFF and alarm reset) are clearly displayed.

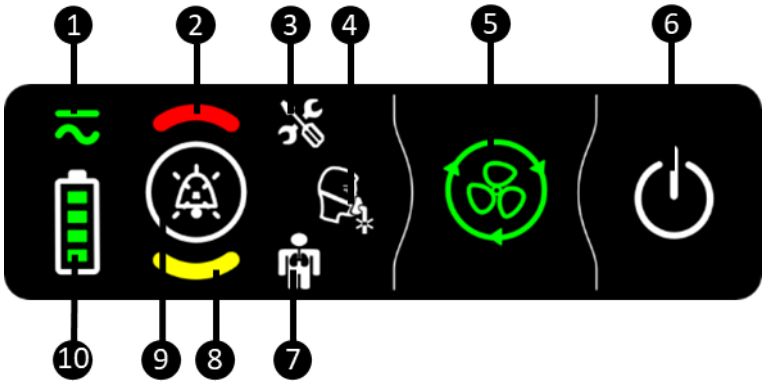


*Figure 9: View of the **EO-150 ventilator** keyboard/menu bar and description of its features*

1. Power source indicator	6. ON / OFF switch
2. High priority alarm indicator	7. Physiological alarm indicator
3. Technical alarm indicator	8. Medium priority alarm indicator
4. Circuit alarm indicator	9. Alarm reset switch
5. Ventilation start / stop switch	10. Battery life indicator

The following list includes all the components of the **EO-150 ventilator** (ref **EO-150VNT)** included in the first shipment :

- A ventilation module: **EO-150 Ventilator module**, ref **EO-VM150**
- A docking station: **EO-1X0 Docking station**, ref **EO-DCK1SLT**
- A power supply (AC/DC): **EO Charger module**, ref **EO-PWRCHRG**
- A double limb circuit adaptor: **EO-150 Double branch adaptor**, ref **EO-DB2-1P-KIT (EO-DB2-1P-INTERFACE + EO-DB2-1P)**
- A leak circuit adaptor plug: **Leak and Mouthpiece adaptor**, ref **EO- LMPADAPT**
- An oxygen connector: **O2 Low Flow Connector**, ref **EO-O2CON**
- A bag for transport: **Transport Bag,** ref **EO-CARBAG1X0**
- A user manual

The **EO-150 ventilato**r, ref EO-150VNT is composed of the following components :

*Table 6: Components of the **EO-150 ventilator***

Description	Reference	Image

EO-150 Ventilator module	EO-VM150	(a)  (b)  (c)  *Figure 10: **EO-150 ventilator** - ventilator module (EO-VM150) (a) front, (b) close up front and (c) back view*
Docking station	EO-DCK1SLT	 *Figure 11: **EO-150 ventilator** - docking station (EO-DCK1SLT)*
Charger module, AC/DC	EO-PWRCHRG	*Figure 12: **EO-150 ventilator** – charger module (EO-PWRCHRG)* 
Double branch adaptor	EO-DB2-1P-KIT	*Figure 13: **EO-150 ventilator** – double branch adaptor (EO-DB2-1P-KIT)* 

Leak and Mouth Piece Adaptor	EO- LMPADAPT	*Figure 14: **EO-150 ventilator** – Leak and mouth piece adaptor (EO-LMPADAPT)* 
Low Flow Oxygen Connector	EO-O2CON	*Figure 15: **EO-150 ventilator** – low flow oxygen connector (EO-O2CON)* 
Transport bag/ case	EO-CARBAG1X0	 *Figure 16: **EO-150 ventilator** – Transport bag/case (EO-CARBAG1X0)*

Software

The software associated to the **EO-150 ventilator** are as follows:

- Software embedded in the device
  - **Motherboard (CPU) software:** software managing the ventilation and communications with the interface systems; Version to date: Motherboard software **C150000702;**
  - **Power supply software**: software that manages the switching of the different power sources and the charging of the internal batteries; Version to date: Power supply software **P150000400.hex**;
  - **Touch interface software (& EO-display app) on the docking station**: software managing the settings and displays of the ventilation parameters; Version to date: **Interface software v3.2.0**.

- Other software associated with the device
  - **EO-toolkit software**: Automated test software for production and after-sales service; Software version to date: **v.3.2.0** ;
  - **Clinical software**: Ventilation data visualisation software; Software version to date: **v.1.6.0**.

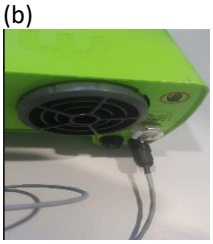
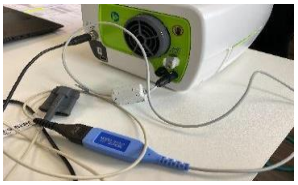
The file "**100-859 Rev.A – EO-150 General Software architecture** " presents the architecture of the different software used.

Accessories provided by EOVE

The **EO-150 ventilator** is compatible with a range of accessories that are listed in the table below:

*Table 7: List and reference of **EO-150 ventilator** accessories provided by EOVE*

Description	Reference	Accessory image	Image of accessory connected to EO-150 ventilator
Accessories			

FIO_2 Cable	O2CELCBL	(a) 	(b)  (c)  *Figure 17: The FIO_2 Cable (O2CELCBL) either (a) alone or (b) and (c) connected to the **EO-150 ventilator***
SPO_2 Cable	EO-SPO2CBL	(a) 	(b)  (c)  *Figure 18: The SPO_2 Cable (EO-SPO2CBL) either (a) alone or (b) and (c) connected to the **EO-150 ventilator***
Proximal Flow sensor	EO-PFLOWS	(a) 	(b)  *Figure 19: The proximal flow sensor (EO-PFLOWS) either (a) alone or (b) connected to the EO-150 ventilator*
Remote Alarm Cable 2 m	EO-ALARMCBL	(a) 	(b)  (c)  *Figure 20: Remote alarm cables (EO-ALARMCBL) (a) alone or connected to the **EO-150 ventilator** with either a (b) 2m long or (c) 4m long cable*
Remote Alarm Cable 4 m	EO-ALARMCBL4		

Upright Brackets	EO-UPRIGHT	(a) 	(b)  *Figure 21: The upright brackets (EO-UPRIGHT) either (a) alone or (b) with the **EO-150 ventilator***
Trolley	EO-TROLLEY	(a) 	(b)  *Figure 22: The trolley (EO-TROLLEY) either (a) alone or (b) with the **EO-150 ventilator***
Nomad Bag (no docking station)	EO-NOMADBAG-EVO	(a) 	*(b)*  *Figure 23: The Nomad Bag (no docking station) (EONOMADBAG-EVO) either (a) alone or (b) with the **EO-150 ventilator***
Travel Bag	EO-TRVELBAG1X0	*Not available*	 *Figure 24: The Nomad Bag (no docking station) (EONOMADBAG-EVO with the **EO-150 ventilator***
EO-BAT9 battery pack			
EO-BAT9 Battery Pack– See EO-BAT9 User manual	EO-BATPCK	(a) 	
Y cable	EO-CPLPACK	(b)	

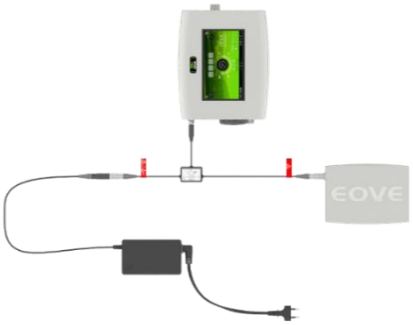
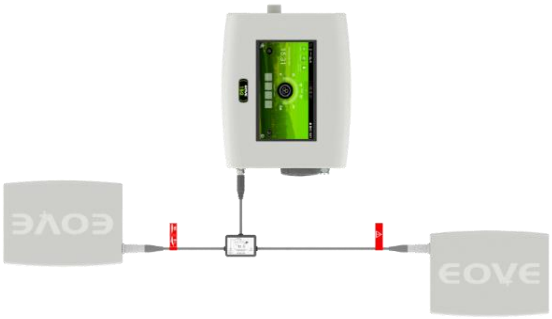
			(d)  (e) 
AC Power/Charger for Y cable	EO-YCBLPWR	(c) 	

*Figure 25: The EO-BAT9 battery pack (EO-BATPK), (a) external battery, (b) Y cable (EO-CPLACK) and (c) AC power/Charger for Y cable (EO-YCBLPWR) (d) all connected to the **EO-150 ventilator** and (e) 2 EO-BAT9 battery packs connected to an **EO-150 ventilator** via a Y cable.*

Accessories not provided by EOVE

The **EO-150** ventilator is compatible with a range of accessories not provided by EOVE that are listed below:

- Humidifier: the **EO-150 ventilator** can be connected to an antibacterial filter (1) and humidifier (2-3). See the detailed description in the IFU manual "**100_23 revDE : user manual_EO-150** " (page 35).

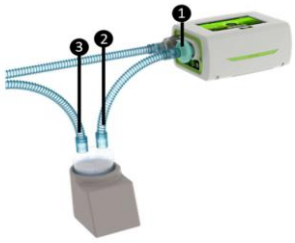


*Figure 26: **EO-150 ventilator** connected to an antibacterial filter (1) and humidifier (2-3).*

- T-connecter and FiO_2 cell (connected to the O2CELCBL cable). See the detailed description of the T-connector and cell installation in the IFU manual "**100_23 revDE : user manual_EO-150** " (page 36-38).

(a) *(b)*

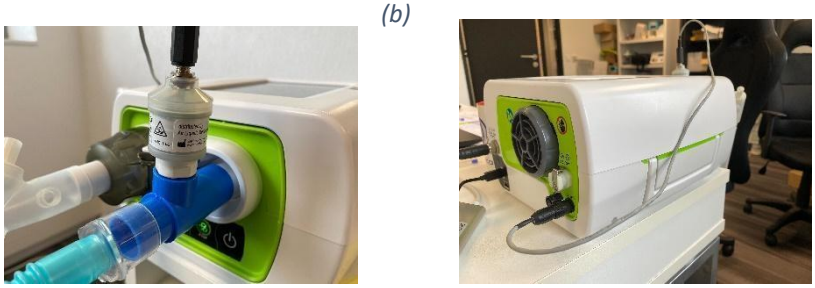


*Figure 27: **EO-150 ventilator** connection to a (a) T-connector and (b) a FiO2 cell*

- SENTEC SPO_2 and Partial Pressure Of Carbon Dioxide (PCO_2) screen (*SenTec* Digital Monitor HB-005752-t). The Sentec sensor (for PCO_2, SPO_2 and heart rate measurements) is connected directly to the Sentec monitor. See the detailed description of the installation in the IFU manual "**100_23 revDE : user manual_EO-150** " (page 39).

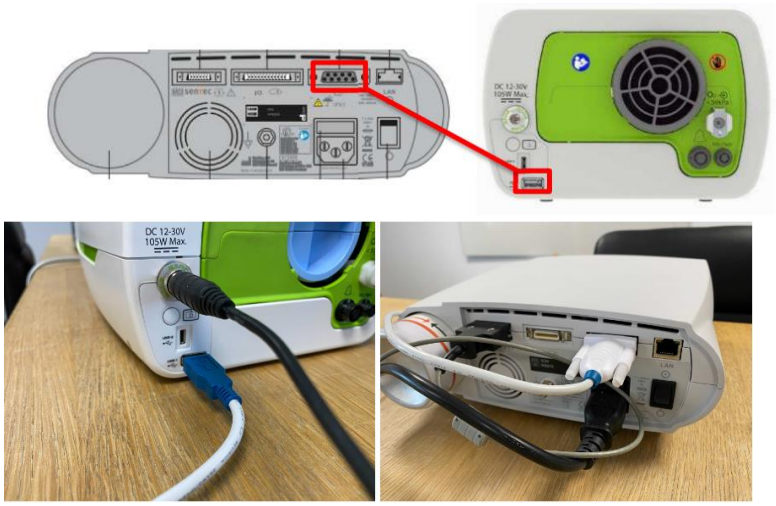


*Figure 28: Rear view of the **EO-150 ventilator** where the SENTEC SPO_2 and PCO_2 screen is connected*

3.2.1.3 Main technical specifications and manufacturing process

3.2.1.3.1 Technical specifications

Ventilation specifications

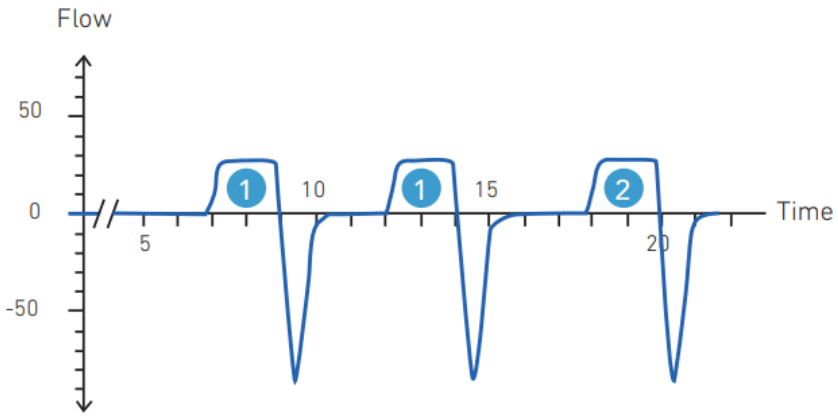
The EO-150 can be used in the following ventilation modes:

- (A)VCV: Volume Assisted Controlled Ventilation (with expiration valve)
- (A)PCV: Pressure Assisted/Controlled Ventilation (with expiration valve)
- PSV: Pressure Support Ventilation (with expiration valve)
- MPV: Mouthpiece Volume Ventilation
- MPP: Mouthpiece Pressure Ventilation
- PSV VT: Pressure Support Ventilation Volume regulated (with expiratory valve)
- V-SIMV: Volume Synchronised Intermittent Mandatory Ventilation (with expiratory Valve)
- P-SIMV: Pressure Synchronised Intermittent Mandatory Ventilation (with expiratory valve)
- CPAP: Continuous Positive Airway Pressure (with leak)

- S(T): Spontaneous Timed (with leak)
- PAC: Pressure Assisted/Controlled (with leak)
- VTS: Volume Target Spontaneous (with leak)
- C-FLOW: Continuous Flow

(A)VCV: Volume Assisted Controlled Ventilation (Valve)

This mode delivers breaths according to the set volume (**VT**), based on a flow control (Rectangle or Decelerated **Flow Slope**). Inspiration lasts a set constant time (**I Time**). Exhalation controls the set exhalation pressure (**PEEP**). Breaths are guaranteed at a set minimum rate (**Rate**). Patient can increase rate by inspiration triggering (**I Trig**.). If a **Sigh** is set, a deeper breath with **I Time** and exhalation time multiplied by the **Sigh VT Coef.** will be delivered every number of breaths corresponding to the set **Sigh Interval.**



1 =Assisted breath triggered by the patient and cycled by the ventilator ; 2=Mandatory breath based on RR
Figure 29: example of (A)VCV waveforms

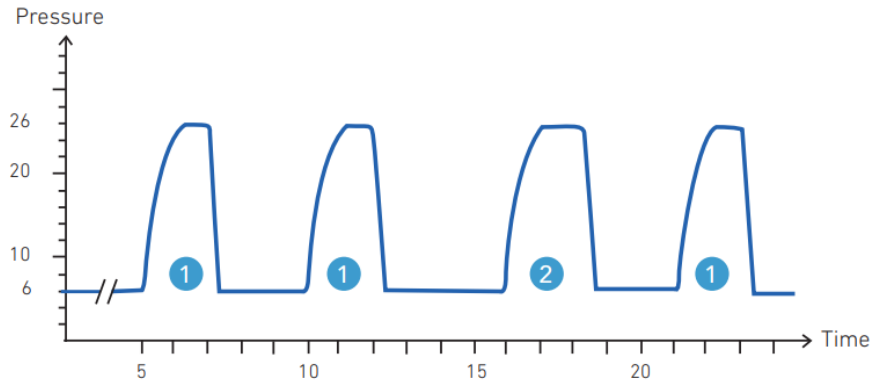
*Table 8: **EO-150 ventilator** settings for (A)VCV mode*

Setting	Adult	Paediatric	Limitations
VT (ml)	300-2500	30-600	None
PEEP (mb)	OFF / 1-25	OFF / 1-20	None
Flow Slope	1 (Rectangle), 2 (Decelerating)		None
Rate (c/min)	5-60	5-80	**Rate** ≤ 45 / **I Time** (I/E ≤ 3/1) *
I Time (s)	0.3-2.5	0.3-2.5	**Rate** ≤ 45 / **I Time** (I/E ≤ 3/1) *
I Trig.	OFF / AUTO / 1-5	OFF / AUTO / 1-5	None
Sigh	ON / OFF	ON / OFF	None
Sigh VT Coef.	1.5 - 2.5	1.5 - 2.5	None
Sigh Interval	50 - 250	50 - 250	None

*A cancellable alarm “Reversed I/E” will trigger when the set I/E ratio exceeds 1/1

(A)PCV: Pressure Assisted Controlled Ventilation (Valve)

This mode delivers breaths according to the set total pressure, **Pres. Control.** added to the set exhalation pressure (**PEEP**). Inspiration lasts a set constant time (**I Time**). Breaths are guaranteed at a set minimum rate (**Rate**). Patient can increase rate by inspiration triggering (**I Trig.**). An optional **VT Target** can be activated.



1 =Assisted breath triggered by the patient and cycled by the ventilator ; 2=Mandatory breath triggered by RR

Figure 30: Example of (A)PCV waveforms

*Table 9: **EO-150 ventilator** settings for (A)PCV mode*

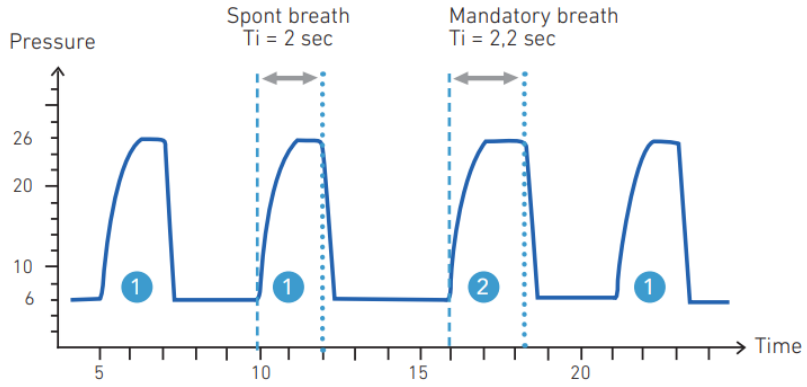
Setting	Adult	Paediatric	Limitations
Pres. Control. (mb)	5-48	5-48	**Pres. Control.** + **PEEP** ≤ 49 mb **Pres. Control.** < **P. Contr. Max**
PEEP (mb)	OFF / 1-25	OFF / 1-20	**Pres. Control.** + **PEEP** ≤ 49 mb **P. Contr. Max** + **PEEP** ≤ 50 mb
Pres. Slope	1-5 (100-500ms)	1-5 (50-250ms)	None
Rate (c/min)	5-60	5-80	**Rate** ≤ 45 / **I Time** (I/E ≤ 3/1) *
I Time (s)	0.3-2.5	0.3-2.5	**Rate** ≤ 45 / **I Time** (I/E ≤ 3/1) *
I Trig.	OFF / AUTO / 1-5	OFF / AUTO / 1-5	None
Vt Target (ml)	OFF / 300-2500	OFF / 30-600	None
P. Contr. Max (mb)	10-49	10-49	Inactive when **Vt Target** is OFF **P. Contr. Max** + **PEEP** ≤ 50 mb **Pres. Control.** < **P. Contr. Max**
VT Target Speed	1-3	1-3	Inactive when **Vt Target** is OFF

*A cancellable alarm “Reversed I/E” will trigger when the set I/E ratio exceeds 1/1

PSV: Pressure Support Ventilation (Valve)

This mode delivers breaths according to the set total pressure, (**Pres. Sup.**) added to the set exhalation pressure (**PEEP**). Inspiration time is variable adapting to patient flow (**E Trig.**). Breaths are guaranteed at a set minimum rate (**Rate**). Patient can increase rate by inspiration triggering (**I Trig.**).

During backup breaths, the set **Backup I Time** defines the inspiration time. If set to AUTO, **Exp. Trig.** still applies to backup breaths. **Exp. Trig**. is allowed between **I Time Min** and **I Time Max**. **I Time Max** has priority on **I Time Min** in case the AUTO conditions are conflicting.



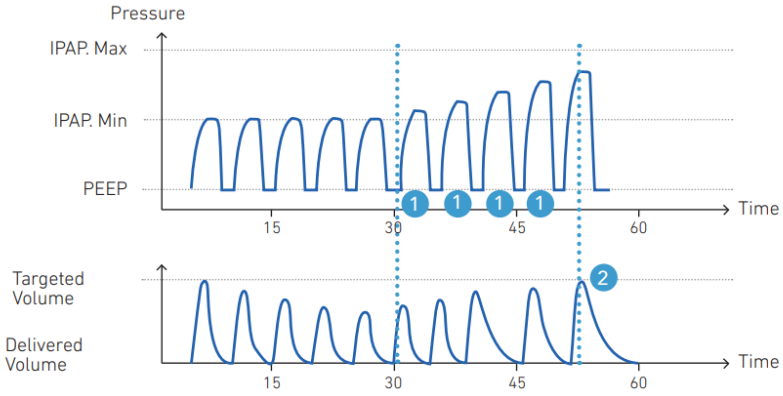
1 =Assisted breath triggered by the patient and cycled by the ventilator ; 2=Mandatory breath triggered by RR
Figure 31: Example of PSV waveforms

*Table 10: **EO-150 ventilator** settings for PSV mode*

Setting	Adult	Paediatric	Limitations
Pres. Support (mb)	5-49	5-49	**Pres. Support** + **PEEP** ≤ 50 mb
PEEP (mb)	OFF / 1-25	OFF / 1-20	**Pres. Support** + **PEEP** ≤ 50 mb
Pres. Slope	1-5(100ms-500ms)	1-5 (50-250ms)	None
Rate (c/min)	5-60	5-80	**Rate** ≤ 30 / **I Time min** (I/E ≤ 1/1) **Rate** ≤ 30 / **Backup I Time** (I/E ≤ 1/1)
I Trig.	AUTO / 1-5	AUTO / 1-5	None
Exp. Trig. (%)	AUTO / 10-90	AUTO / 10-90	None
Backup I Time (s)	AUTO / 0.3-2.5	AUTO / 0.3-2.5	**Rate** ≤ 30 / **Backup I Time (**I/E ≤ 1/1)
I Time Min (s)	AUTO / 0.3-2.5	AUTO / 0.3-2.5	**Rate** ≤ 30 / **I Time min** (I/E ≤ 1/1) **I Time Min** ≤ **I Time Max** **I Time Min** AUTO = **Press Slope** + 100 ms
I Time Max (s)	AUTO / 0.3-2.5	AUTO / 0.3-2.5	**I Time Min** ≤ **I Time Max** **I Time Max** AUTO = 30 / **Rate**

PSV VT: Pressure Support Ventilation with VT Target (Valve)

This mode delivers breaths according to the set target volume (**VT**), based on pressure control adapting breath by breath, between the set total pressure limits (**Pres Sup Min and P Sup Max**) added to the set exhalation pressure (**PEEP**). **VT Target Speed** adapts the maximum pressure increments between two breaths. Inspiration time is variable according to patient flow (**E Trig**). Breaths are guaranteed at a set minimum rate (**Rate**). Patient can increase rate by inspiration triggering (**I Trig**.). During backup breaths, the set **Backup I Time** defines the inspiration time. If set to AUTO, **E trig.** still applies to backup breaths. **E Trig.** is allowed between **I Time Min** and **I Time Max**. **I Time Max** has priority on **I Time Min** in case the AUTO conditions are conflicting.



1 =Pressure increment breath by breath ; 2=Targeted volume reached

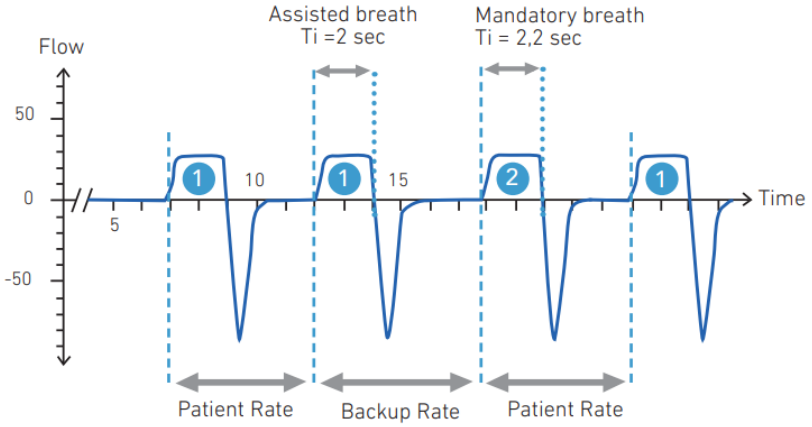
Figure 32: Example of PSV VT waveforms

*Table 11: **EO-150 ventilator** settings for PSV VT mode*

Setting	Adult	Paediatric	Limitations
Vol. Target (ml)	300-2500	30-600	None
Pres Sup Min (mb)	5-48	5-48	**Pres Sup Min** < **Pres Sup Max**
Pres Sup Max (mb)	10-49	10-49	**Pres Sup Min** < **Pres Sup Max** **Pres Sup Max** + **PEEP** ≤ 50 mb
PEEP (mb)	OFF / 1-25	OFF / 1-20	**Pres Sup Max** + **PEEP** ≤ 50 mb
Pres. Slope	1-5 (100-500ms)	1-5 (50-250ms)	None
Rate (c/min)	5-60	5-80	**Rate** ≤ 30 / **I Time min** (I/E ≤ 1/1) **Rate** ≤ 30 / **Backup I Time** (I/E ≤ 1/1)
I Trig.	AUTO / 1-5	AUTO / 1-5	None
E Trig. (%)	AUTO / 10-90	AUTO / 10-90	None
VT Target Speed	1-3	1-3	None
Backup I Time (s)	AUTO / 0.3-2.5	AUTO / 0.3-2.5	**Rate** ≤ 30 / **Backup I Time** (I/E ≤ 1/1)
I Time Min (s)	AUTO / 0.3-2.5	AUTO / 0.3-2.5	**Rate** ≤ 30 / **I Time min** (I/E ≤ 1/1) **I Time Min** ≤ **I Time Max** **I TIME Min** AUTO = **Press Slope** + 100 ms
I Time Max (s)	AUTO / 0.3-2.5	AUTO / 0.3-2.5	**I Time Min** ≤ **I Time Max** **I Time Max** AUTO = 30 / **Rate**

V-SIMV: Volume Synchronised Intermittent Ventilation (Valve)

This mode delivers mandatory breaths according to the set volume (**VT**), at set minimum rate (**Rate**) and a set constant inspiration time (**I Time**). Patient can trigger additional spontaneous breaths (**I Trig**.) according to the set total pressure (**Pres. Support**) added to the set exhalation pressure (**PEEP**) with a variable inspiration time adapting to patient flow (**E Trig**). During spontaneous breaths, **E Trig**. is allowed between **I Time Min** and **I Time Max**. **I Time Max** has priority on **I Time Min** in case the AUTO conditions are conflicting.



1 =Assisted breath triggered by the patient ; 2=Mandatory breath based on RR but synchronised with patient

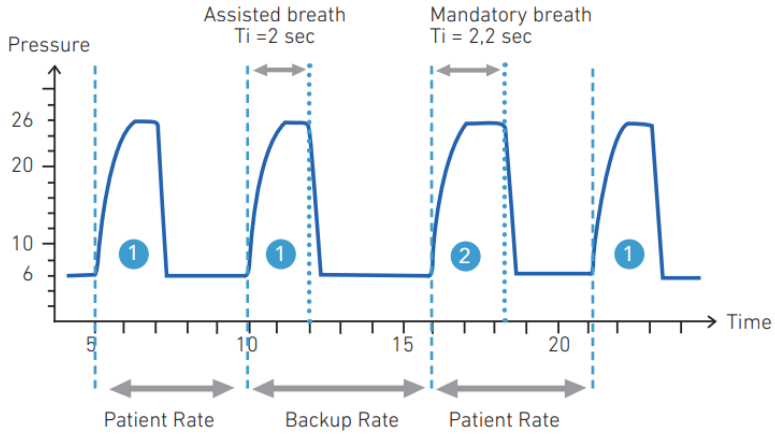
Figure 33: Example of V-SIMV waveforms

*Table 12: **EO-150 ventilator** settings for V-SIMV mode*

Setting	Adult	Paediatric	Limitations
VT (ml)	300-2500	30-600	None
Pres. Support (mb)	5-49	5-49	**Pres. Support** + **PEEP** ≤ 50 mb
PEEP (mb)	OFF / 1-25	OFF / 1-20	**Pres. Support** + **PEEP** ≤ 50 mb
Pres. Slope	1-5 (100-500ms)	1-5 (50-250ms)	None
Rate (c/min)	5-40	5-60	**Rate** ≤ 30 / **I Time** (I/E ≤ 1/1) **Rate** ≤ 30 / **I Time min** (I/E ≤ 1/1)
I Time (s)	0.3-2.5	0.3-2.5	**Rate** ≤ 30 / **I Time** (I/E ≤ 1/1)
I Trig.	AUTO / 1-5	AUTO / 1-5	None
E Trig.(%)	AUTO / 10-90	AUTO / 10-90	None
I Time Min (s)	AUTO / 0.3-2.5	AUTO / 0.3-2.5	**I Time Min** ≤ **I Time Max** **Rate** ≤ 30 / **I Time min** (I/E ≤ 1/1) **I TIME Min** AUTO = **Press Slope** + 100 ms
I Time Max (s)	AUTO / 0.3-2.5	AUTO / 0.3-2.5	**I Time Min** ≤ **I Time Max** **I Time Max** AUTO = 30 / **Rate**

P-SIMV: Pressure Synchronised Intermittent Ventilation (Valve)

This mode delivers mandatory breaths according to the set total pressure (**Pres. Control.**) added to the set exhalation pressure (**PEEP**) at set minimum rate (**Rate**) at a set constant inspiration time (**I Time**). Patient can trigger additional spontaneous breaths (**I Trig**.) according to the set total pressure (**Pres. Support**) added to the set exhalation pressure **(PEEP**) with a variable inspiration time adapting to patient flow (**E Trig**). During spontaneous breaths, **E Trig**. is allowed between **I Time Min** and **I Time Max**. **I Time Max** has priority on **I Time Min** in case the AUTO conditions are conflicting.



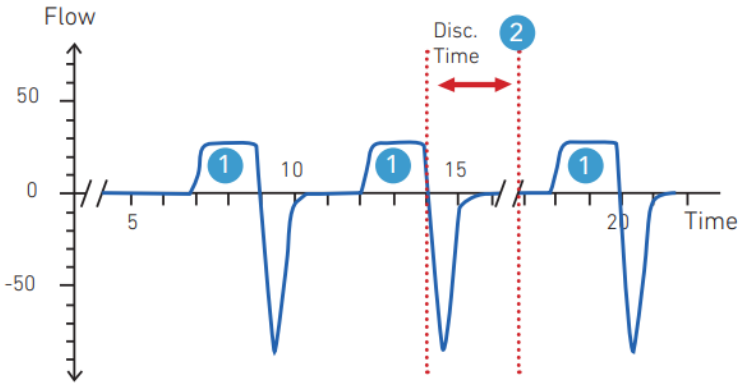
1 =Assisted breath triggered by the patient ; 2=Mandatory breath based on RR but synchronised with patient
Figure 34: Example of P-SIMV waveforms

*Table 13: **EO-150 ventilator** settings for P-SIMV mode*

Setting	Adult	Paediatric	Limitations
Pres. Control. (mb)	5-49	5-49	**Press. Control.** + **PEEP** ≤ 50 mb
Pres. Support (mb)	5-49	5-49	**Pres. Support** + **PEEP** ≤ 50 mb
PEEP (mb)	OFF / 1-25	OFF / 1-20	**Press. Control.** + **PEEP** ≤ 50 mb **Press. Support** + **PEEP** ≤ 50 mb
Pres. Slope	1-5 (100-500ms)	1-5 (50-250ms)	None
Rate (c/min)	5-40	5-60	**Rate** ≤ 30 / **I Time** (I/E ≤ 1/1) **Rate** ≤ 30 / **I Time min** (I/E ≤ 1/1)
I Time (s)	0.3-2.5	0.3-2.5	**Rate** ≤ 30 / **I Time** (I/E ≤ 1/1)
I Trig.	AUTO / 1-5	AUTO / 1-5	None
E Trig. (%)	AUTO / 10-90	AUTO / 10-90	None
I Time Min (s)	AUTO / 0.3-2.5	AUTO / 0.3-2.5	**Rate** ≤ 30 / **I Time min** (I/E ≤ 1/1) **I Time Min** ≤ **I Time Max** **I TIME Min** AUTO = **Press Slope** + 100 ms
I Time Max (s)	AUTO / 0.3-2.5	AUTO / 0.3-2.5	**I Time Min** ≤ **I Time Max** **I Time Max** AUTO = 30 / **Rate**

MPV: Mouthpiece Volume Ventilation (Valve or no valve)

This mode delivers breaths according to the set volume (**VT**), based on a flow control (**Rectangle or Decelerated Flow Ramp**). Inspiration lasts a set constant time (**I Time**). The minimum rate (**Rate**) is an optional setting. Exhalation control is delivering the set flow (**Bias Flow**), based on a flow control. Patient triggering (**I. Trig**.) and alarms are specific to the mouthpiece configuration needs.



1 =Breath triggered by the patient ; 2=Disconnection alarm

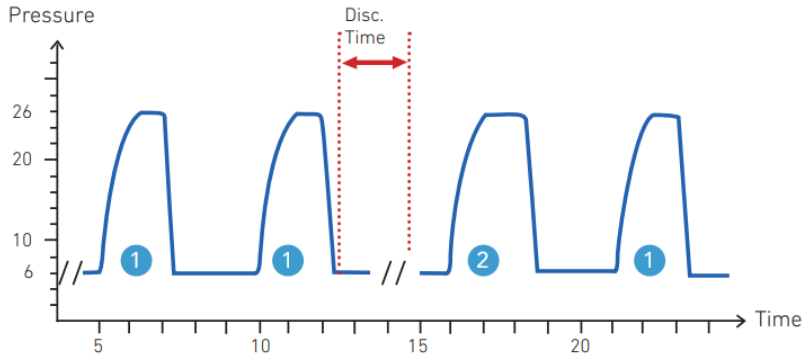
Figure 35: Example of MPV waveforms

*Table 14: **EO-150 ventilator** settings for MPV mode*

Setting	Adult	Paediatric	Limitations
VT (ml)	100-2500	100-600	None
Bias Flow (l/min)	OFF / 1-20 l/min	OFF / 1-20 l/min	None
Flow Slope	1 (Rectangle), 2 (Decelerating)		None
Rate (c/min)	OFF / 5-60	OFF / 5-80	**Rate** ≤ 30 / **I Time** (I/E ≤ 1/1)
I Time (s)	0.3-2.5	0.3-2.5	**Rate** ≤ 30 / **I Time** (I/E ≤ 1/1)
I Trig.	AUTO / 1-5	AUTO / 1-5	None

MPP: Mouthpiece Pressure Ventilation (Valve or no valve)

This mode delivers breaths according to the set pressure (**Pres. Control.**), based on a pressure control. Inspiration lasts a set constant time (**I Time**). The minimum rate (**Rate**) is an optional setting. Exhalation control is delivering the set flow (**Bias Flow**), based on a flow control. Patient triggering (**I Trig**.) and alarms are specific to the mouthpiece configuration needs.



1 =Breath triggered by the patient ; 2=Disconnection alarm

Figure 36: Example of MPP waveforms

*Table 15: **EO-150 ventilator** settings for MPP mode*

Setting	Adult	Paediatric	Limitations
Pres. Control. (mb)	5-49	5-49	None
Bias Flow (l/min)	OFF / 1-20 l/min	OFF / 1-20 l/min	None
Pres. Slope	1-5 (100-500ms)	1-5 (50-250ms)	None
Rate (c/min)	OFF / 5-60	OFF / 5-80	**Rate** ≤ 30 / **I Time** (I/E ≤ 1/1)
I Time (s)	0.3-2.5	0.3-2.5	**Rate** ≤ 30 / **I Time** (I/E ≤ 1/1)
I Trig.	AUTO / 1-5	AUTO / 1-5	None

CPAP: Continuous Positive Airway Pressure (Leak)

This mode delivers continuous pressure to the patient. All breaths in this mode are spontaneous breaths.

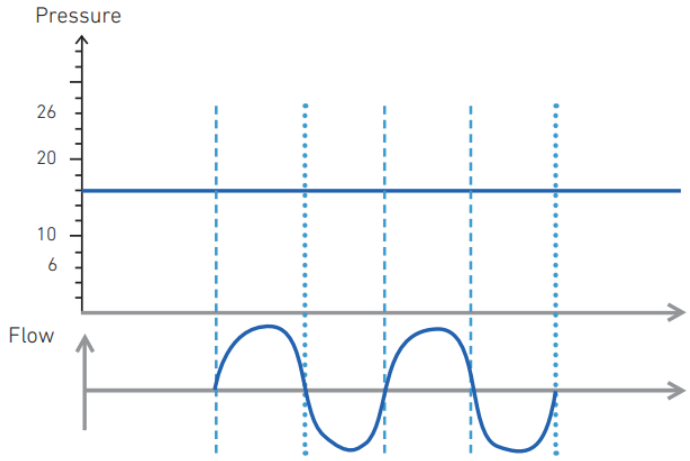


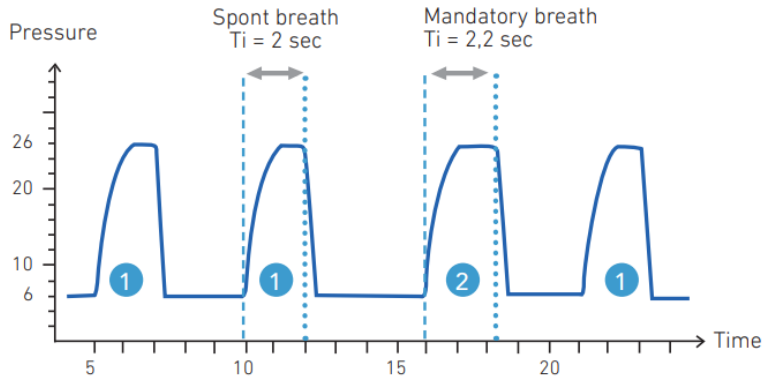
Figure 37: Example of CPAP waveforms

*Table 16: **EO-150 ventilator** settings for CPAP mode*

Setting	Adult	Paediatric	Limitations
CPAP Pressure (mb)	4-20	4-20	None

S(T): Spontaneous Timed (Leak)

This mode delivers breaths according to the set inspiration pressure (**IPAP**) and set exhalation pressure (**EPAP**). Inspiration time is variable adapting to patient flow (**E. Trig.**). Breaths are guaranteed at a set minimum rate (**Rate**), unless **Rate** is turned OFF. Patient can increase rate by inspiration triggering (**I. Trig.**). On backup breaths, the set **Backup I Time** defines the inspiration time. If set to AUTO, **E trig.** still applies to backup breaths. **E Trig**. is allowed between **I Time Min** and **I Time Max**. **I Time Max** has priority on **I Time Min** in case the AUTO conditions are conflicting.



1 =Assisted breath triggered and cycled by the patient ; 2=Mandatory breath triggered by backup RR

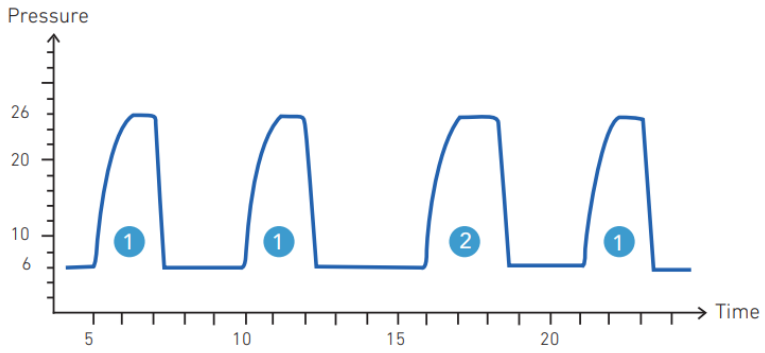
Figure 38: Example of S(T) waveforms

*Table 17: **EO-150 ventilator** settings for S(T) mode*

Setting	Adult	Paediatric	Limitations
IPAP (mb)	6-50	6-50	**IPAP** ≥ **EPAP** + 2
EPAP (mb)	4-25	4-20	**IPAP** ≥ **EPAP** + 2
Pres. Slope	1-5 (100-500ms)	1-5 (50-250ms)	None
Rate (c/min)	OFF / 5-60	OFF / 5-80	**Rate** ≤ 30 / **I Time min** (I/E ≤ 1/1) **Rate** ≤ 30 / **Backup I Time** (I/E ≤ 1/1)
I Trig.	AUTO / 1-5	AUTO / 1-5	None
E Trig. (%)	AUTO / 10-90	AUTO / 10-90	None
Backup I Time (s)	AUTO / 0.3-2.5	AUTO / 0.3-2.5	**Rate** ≤ 30 / **Backup I Time** (I/E ≤ 1/1) Inactive if **Rate** is OFF
I Time Min (s)	AUTO / 0.3-2.5	AUTO / 0.2-2.5	**Rate** ≤ 30 / **I Time min** (I/E ≤ 1/1) **I Time Min** ≤ **I Time Max** **I TIME Min** AUTO = **Press Slope** + 100 ms
I Time Max (s)	AUTO / 0.3-2.5	AUTO / 0.3-2.5	**I Time Min** ≤ **I Time Max** **I Time Max** AUTO = 30 / **Rate** If **Rate** is OFF, **I Time Max** AUTO corresponds to 2.5 s in Adult, 1.5 s in Paediatric, and 1 s in Newborn

PAC: Pressure Assisted Controlled (Leak)

This mode delivers breaths according to the set inspiration pressure (**IPAP**) and set exhalation pressure (**EPAP**). Inspiration lasts a set constant time (**I Time**). Breaths are guaranteed at a set minimum rate (**Rate**). Patient can increase rate by inspiration triggering (**I Trig**.). An optional **VT Target** can be activated.



1 =Assisted breath triggered by patient and cycled by ventilator ; 2=Mandatory Breath triggered by RR
Figure 39: Example of PAC waveforms

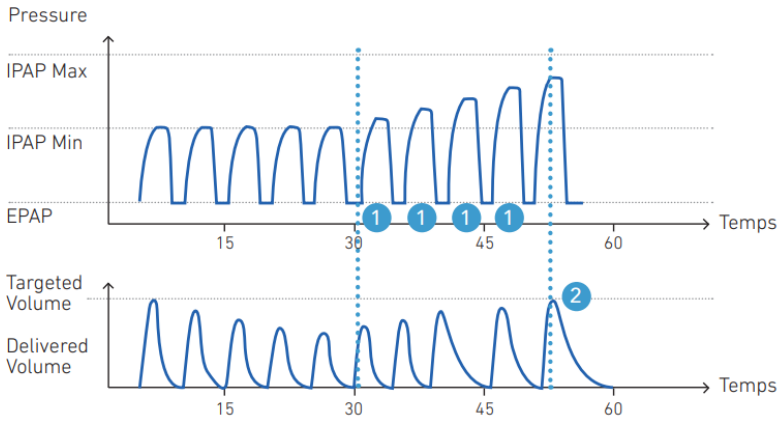
*Table 18: **EO-150 ventilator** settings for PAC mode*

Setting	Adult	Paediatric	Limitations
IPAP (mb)	6-49	6-49	**IPAP** ≥ **EPAP** + 2
EPAP (mb)	4-25	4-20	**IPAP** ≥ **EPAP** + 2
Pres. Slope	1-5 (100-500ms)	1-5(50-250ms)	None
Rate (c/min)	5-60	5-80	**Rate** ≤ 45 / **I Time** (I/E ≤ 3/1)*
I Time (s)	0.3-2.5	0.2-2.5	**Rate** ≤ 45 / **I Time** (I/E ≤ 3/1)*
I Trig.	OFF / AUTO / 1-5	OFF / AUTO / 1-5	None
Vt Target (ml)	OFF / 300-2500	OFF / 30-600	None
IPAP Max (mb)	7-50	7-50	Inactive when **VT Target** is OFF
VT Target Speed	1-3	1-3	Inactive when **VT Target** is OFF

*A cancellable alarm “Reversed I/E” will trigger when the set I/E ratio exceeds 1/1

VTS: Volume Target Spontaneous mode (Leak)

This mode delivers breaths according to the set volume (**Vol. Target**) based on pressure control adapting breath by breath, between the set pressure limits (**IPAP Min** and **IPAP Max**). **VT Target Speed** adapts the maximum pressure increments between two breaths. Inspiration time is variable adapting to patient flow (**Exp. Trig.**). Breaths are guaranteed at a set minimum rate (**Rate**). Patient can increase rate by inspiration triggering (**I Trig.**). On backup breaths, the set Backup I Time defines the inspiration time. If set to AUTO, exhalation triggering (**Exp. Trig.**) still applies to backup breaths. **Exp. Trig**. is allowed between **I Time Min** and **I Time Max**. **I Time Max** has priority on **I Time Min** in case the AUTO conditions are conflicting.



1 =Pressure increment breath by breath ; 2 =Targeted volume reached
Figure 40: Example of VTS waveforms

*Table 19: **EO-150 ventilator** settings for VTS mode*

Setting	Adult	Paediatric	Limitations
Vol. Target (ml)	300-2500	30-600	None
IPAP Min (mb)	6-49	6-49	**IPAP Max** ≥ **IPAP Min** + 5 **IPAP Min** ≥ **EPAP** + 2
IPAP Max (mb)	7-50	7-50	**IPAP Max** ≥ **IPAP Min**
EPAP (mb)	4-25	4-20	**IPAP Min** ≥ **EPAP** + 2
Pres. Slope	1-5 (100-500ms)	1 -5(50-250ms)	None
Rate (c/min)	5-60	5-80	**Rate** ≤ 30 / **I Time min** (I/E ≤ 1/1) **I Time Min** ≤ **I Time Max**
I Trig.	AUTO / 1-5	AUTO / 1-5	None
Exp Trig. (%)	AUTO / 10-90	AUTO / 10-90	None
Backup I Time (s)	AUTO / 0.3-2.5	AUTO / 0.3-2.5	**Rate** ≤ 30 / **Backup I Time** (I/E ≤ 1/1)
VT Target Speed	1-3	1-3	None
I Time Min (s)	AUTO / 0.3-2.5	AUTO / 0.2-2.5	**Rate** ≤ 30 / **I Time min** (I/E ≤ 1/1) **I Time Min** ≤ **I Time Max** **I TIME Min** AUTO = **Press Slope** + 100 ms
I Time Max (s)	AUTO / 0.3-2.5	AUTO / 0.3-2.5	**I Time Min** ≤ **I Time Max** **I Time Max** AUTO = 30 / **Rate**

C-FLOW: Continuous Flow (Leak)

This mode delivers continuous flow to the patient. The set flow (**Flow**) is delivered continuously through the humidifier and nasal cannula. If the maximum pressure (**Pres. Max**) is reached, the device will still deliver flow but within the limit of this pressure.

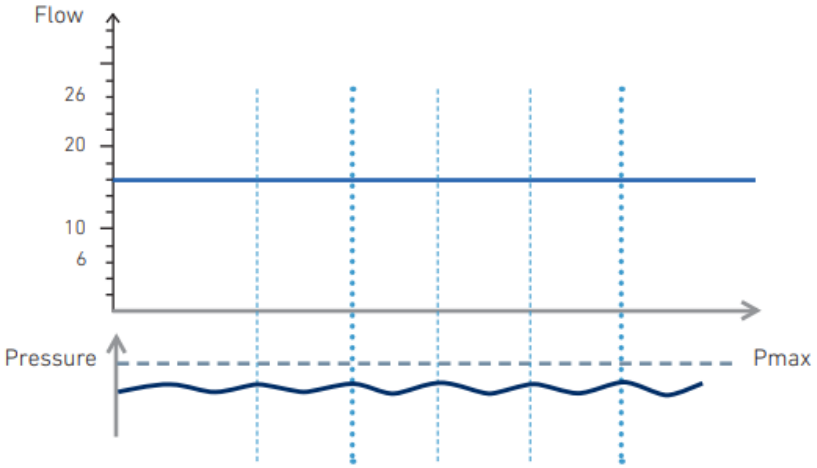


Figure 41: Example of C-FLOW waveforms

*Table 20: **EO-150 ventilator** settings for C-FLOW mode*

Settings	Adult	Paediatric	Limitations
Flow (l/min)	10-60	2-25	None

Accuracy of ventilation settings

- Valve volumes: ± (5 ml + 10%) under BTPS conditions
- MPV volumes: ± (10 ml + 15%) under BTPS conditions
- Leak volumes: ± (10 ml + 10%) under BTPS conditions
- Sigh Volumes: +/- (10 ml + 20%) under BTPS conditions
- Pressure: ± (1 mb + 10%)
- Time: ± 0.1 s
- Rate: ± 1 breath/min
- Flow: ± (0.5 l/min + 10%)

Measurement uncertainties (measurement control device)

- Pressure: ± 0.75% or ± 0.1 mb*
- Flow: ± 1.9% or ± 0.1 l/min*
- Volumes: ± 2% or ± 0.2 ml*
- Time: ± 0.02 s

*Whichever is greater

According to ISO 80601-2-72 standard, all volume, flow, leak specifications should be expressed in STPD conditions apart from VBS (Ventilator Breathing System) characteristics expressed in BTPS at the absolute pressure of the VBS.

Monitored parameter specifications

*Table 21: **EO-150 ventilator** parameter specifications*

Parameter	Range	Display method / Filtering
Peak Inspiratory Pressure (PIP)	0 to 99 mbar	Computed for each inspiration
Positive End Expiratory Pressure (PEEP)	0 to 60 mbar	Computed for each exhalation
Inspiratory Tidal Volume (VTI)	0 to 4000 ml	Computed for each inspiration
Exhalation Tidal Volume (VTE)	0 to 4000 ml	Computed for each exhalation
Total Breath Rate (Res. Rate)	1 to 99.9 bpm	Computed for each 4 breaths
I/E Ratio (I/E)	33.3:1 to 1:99.9	Computed for each breath
Inspiratory Time (Insp. Time)	0.1 to 9.9 s	Computed for each inspiration
Exhalation Time (Exp. Time)	0.3 to 59.9 s	Computed for each exhalation
I Peak Flow	0 to 100 l/min	Computed for each inspiration
E Peak Flow	0 to 100 l/min	Computed for each exhalation
Inspiratory Minute Volume (MV)	0 to 99.9l	Computed for each breath
Leak: Leak modes Valve modes	 0 to 200 l/min 0 to 100 l/min	Computed for each breath
FiO2	21% to 100%	Computed for each breath
SpO2	80% to 100%	According to NONIN or Sentec
Pulse Rate	30-250 (Sentec) 18-300 (NONIN)	According to NONIN or Sentec
PCO2	0-200	According to Sentec

A monitored value displayed as "--" means that the measurement is not available or invalid. Rounded values for readings.

Accuracy of monitoring data

- Inspired volume in valve modes: ± (5 ml + 10%)
- Expired volume in valve modes: ± (5 ml + 20%)
- Leak volume: ± (10 ml + 10%)
- Pressure: ± (2 mb + 4%)
- Time: ± 0.1 s
- I/E: Calculation based on Inspiratory Time and Exhalation Time
- Rate: ± 1 breath/min
- Leak: ± (2 l/min + 15%)
- Peak flow: +/- (2l/min + 20%)
- Minute volume: +/- (0,2L + 10%)
- FIO2: ± 3%
- SPO2: According to NONIN or Sentec specifications
- Pulse Rate: According to NONIN or Sentec specifications
- PCO2: According to Sentec specifications

Alarm parameter specifications

Alarm sound level: 55 - 75 dB ± 10%
The ventilator has the following alarm settings in specific ventilation modes:

*Table 22: **EO-150 ventilator** alarm settings*

Settings	Adult	Paediatric	Modes
Pres. Min (mb)*	2-55 1-45	5-55 1-45	(A)VCV, MPV, VSIMV C-FLOW
Pres. Max (mb)*	10-80 7-50	10-80 7-50	(A)VCV, MPV, VSIMV C-FLOW
VTI Min (ml)	OFF / 50-2490	OFF / 20-590	All except (A)VCV, MPV, MPP, C-FLOW
VTI Max (ml)	OFF / 310-3000	OFF / 40-800	(A)PCV, PSV, PSV VT, VSIMV, PSIMV
VTE Min (ml)	OFF / 50-2490	OFF / 20-590	All valve modes
VTE Max (ml)	OFF / 310-3000	OFF / 40-800	All valve modes
MV Min	OFF / 1-25	OFF / 0.5-6	All except (A)VCV, C-FLOW
Res. Rate Min	OFF / 6-65	OFF / 6-85	PSV, PSV VT, ST, VTS, CPAP
Res. Rate Max	OFF / 10-70	OFF / 20-90	All except MPV, MPP, CPAP, C-FLOW
FIO2 Min	OFF / 18-80	OFF / 18-80	All
FIO2 Max	OFF / 30-100	OFF / 30-100	All
SPO2 Min	OFF / 80-95	OFF / 80-95	All
Leak Max	OFF / 10-100	OFF / 10-100	All Leak modes except C-FLOW
Disc. Time	AUTO / 5-120	AUTO / 5-60	All except MPV, MPP, C-FLOW, CPAP
Disc. Time	OFF / 5-120	OFF / 5-60	C-FLOW
Disc. Time	5-120	5-60	CPAP
Disc. Time	OFF / 5-900	OFF / 5-900	MPV, MPP
*PWmax and PWmin according to ISO 10651-2 / ISO 80601-2-72			

Power specifications

AC Inlet Voltage	100-240V
AC Inlet Power	1.6 A max
AC Inlet Frequency	50-60 Hz
DC inlet voltage Max current	12 to 30 V 2.5 to 5.8 A
Power	105 W maximum (peaks) 70 W nominal
Module Embedded battery life	5 hrs

Internal battery (not replaceable by user): capacity voltage discharge current	Lithium-ion 2.8 / 2.95 Ah 21,6 V nominal 7 A max
Interface/touchscreen start up time	< 60 s
Ventilator unit start up time	5 seconds

Environmental specifications

Storage and transport conditions:

Ambient temperature	From -20°C à +60°C.
Relative humidity	From 10% à 95%, (non-condensing)

Operating conditions:

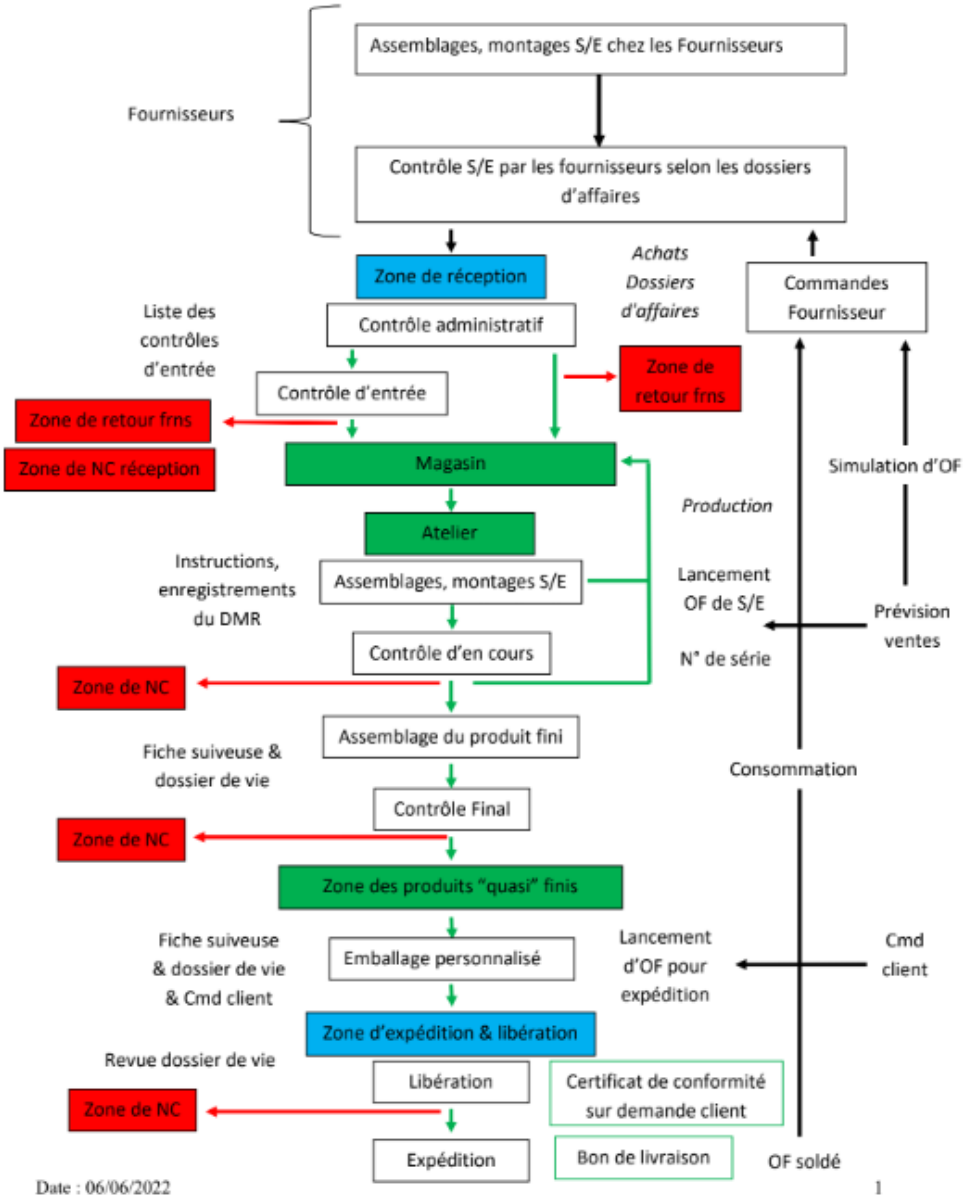
Ambient temperature	From +5°C to +40°C (after conditioning at 23° for 20 minutes)
Relative humidity	From 10% à 95%, (non-condensing)
Atmospheric pressure	From 660 hPa to 1100 hPa. (by default, EO150 compensates for atmospheric pressure variations related to altitude up to 3000 m)
O2 pressure source	O2 pressure source: up to 50 Kpa with flow up to 20 l/min and flexible tubing used. (from hospital O2 network, always use a flow or pressure limiter)

Breathing system specifications

Inspiratory resistance at 60 l/min Ventilation stopped / Failure	< 3 mb
Expiratory resistance at 60 l/min Ventilation stopped / Failure	< 3 mb
Breathing system Compliance	< 5 ml/cmH2O
Anti-bacterian Filter caracteristics	Resistance < 2 mb @ 60 l/min Dead space < 120 ml

3.2.1.3.2 Manufacturing

Manufacturing site: EOVE - 4, boulevard Lucien Favre - Immeuble Poincaré - 64 000 PAU.
The manufacturing flowchart is presented below:



(Cmd: Order, Frns: Supplier, NC: Non-Conformity, OF: Production Order and S/E: Sub-assembly)
*Figure 42: Flowchart of the **EO-150 ventilator** manufacturing process.*

See document "**ENR-PRO 14 Rev C Inspection tests EO-150 in Manufacturing process**" for details of the controls and validated manufacturing processes carried out.

Description of the manufacturing methods and controls performed
The manufacturing methods for the subcontractors are machining, plastic injection and card wiring.
The tests entrusted to the subcontractors are those relating to the wiring of electronic boards.
See below the references of the associated control documents:

- **EO-150 ventilator** module CPU and turbine boards:
  - FAB100-029 - E0151 CPU board test instruction

- FAB100-101 - EO151 CPU Board Test Report
- FAB100-102 - EO151 Turbine Board Test Report

- EO-Display Station Board
  - FAB100-107 - EO Display CPU Board Test Instruction
  - FAB100-104 - EO Display CPU Board Test Report
  - FAB100-105 - Test report for the wifi card

The manufacturing methods at EOVE are assembly and control:
Below are the references of the control documents at the assembly and final control level:
- FAB100-034 control during the assembly of the ventilator module
- FAB100-037 check during assembly of the docking station
- FAB100-166 check during assembly of the exhalation valve
- FAB100-040 final check of the EO150 ventilation module
- FAB100-037 final check of the docking station

For current versions, see Current Manufacturing File: "**FAB100-001 Rev. DV**" + file "**ENR-PRO 14 Rev.C Inspection tests EO-150 in Manufacturing process**".

Description of manufacturing environments: Not applicable. No specific manufacturing environment.

There are no subcontracted processes. However, the major subcontractors are listed below with their respective trade and know-how.

Identification of major subcontractor(s) :
- ISO 13 485 certified :
  - **Airfan / Airtechnologies** - 3 av Léon Foucault 31770 Colomiers (Turbine Design and Manufacturing)
  - **VLAD** - 400, rue Emile Dewoitine - 37 210 - Parçay-Mestay (Battery design and manufacture)
  - **INOVELEC** - Allée Jacques Duclos -ZI du Landry - 24750 - Boulazac (Electronic card wiring)
  - **BOURSIER SOGREG** - 5 rue Harispe - Avenue de l'Ursuya - 64250 CAMBO-LES-BAINS (plastic-shell injection)

- ISO 9001 certified:
  - **Martin Technologie** - 22, rue Henri Gandon - BP 80105 - 49430 - Lézigné (Design and manufacture of keyboards / lexan)
  - **EFFIPLAST** - Chemin d'Auguste, 33610 Cestas (Plastic injection)

- Others :
  - **Mécagil-Lebon** - ZA ETIC, 47 rue de l'Aqueduc- 77430 Champagne-sur-Seine (Machining of pneumatic blocks)

For the selection of major (also called "critical") subcontractors, an on-site audit is required (see file "**PR09"**). The identification of these major subcontractors and the impact of their activities in the product production process was carried out through the results of the Manufacturing FMECA (document "**FAB100-002"**).

3.2.1.3.3 Packaging

The primary packaging material is the packing carton. See document "**100-79 Rev.H** Raw **materials and Critical components List**". There are no manufacturing residues.
Primary packaging specification:
The medical device is placed in the carrying case, which is itself placed in a shipping cardboard box with the plan referenced in the file "**110-000 Rev. I**".

A detailed list of symbols present on the device/packaging is available in the user manual file "**manual_eove_150_en_US revDE**". Packaging process Validation: Not applicable. No process to be validated.

3.2.2 Mode of action

The **EO-150 ventilator** is an artificial respirator that provides ventilatory assistance to patients with respiratory insufficiency. This device is mainly intended to be used at the patient's home. It is initially installed by a healthcare provider who has been commissioned by a physician to fit the patient with the device and adjust ventilation parameters to the patient's needs.

The **EO-150 ventilator** can be used with five different circuits, as seen below. Breathing circuits may be 10, 15 or 22 mm in diameter.
See the following table to select suitable circuits and settings for different patient types.

Table 23: Ventilation circuit type depending on patient typology

Air volume	Patient	Circuit Diameter
30 ml to 300 ml	Paediatric	10 mm or 15 mm
> 300 ml	Adult	15 mm or 22 mm

The five types of circuits that can be used with the **EO-150 ventilator** are listed below:

- Single Limb with valve Single limb circuit with expiratory valve (expiratory valve integrated into the circuit)
- Single Limb with valve + proximal flow : Single limb circuit with expiratory valve and proximal flow sensor
- Double Limb (with adapter) : Double limb circuit (expiratory valve integrated into the adapter)
- Single limb with Leak : Single limb circuit with intentional leak using proximal free plug or proximal adaptor
- Single limb with Mouthpiece : Single limb circuit with mouthpiece using proximal free plug or proximal adaptor

The EO-150 can be used in the following ventilation modes:

- (A)VCV: Volume Assisted Controlled Ventilation (with expiration valve)
- (A)PCV: Pressure Assisted/Controlled Ventilation (with expiration valve)
- PSV: Pressure Support Ventilation (with expiration valve)
- MPV: Mouthpiece Volume Ventilation
- MPP: Mouthpiece Pressure Ventilation
- PSV VT: Pressure Support Ventilation Volume regulated (with expiratory valve)
- V-SIMV: Volume Synchronised Intermittent Mandatory Ventilation (with expiratory Valve)
- P-SIMV: Pressure Synchronised Intermittent Mandatory Ventilation (with expiratory valve)
- CPAP: Continuous Positive Airway Pressure (with leak)
- S(T): Spontaneous Timed (with leak)
- PAC: Pressure Assisted/Controlled (with leak)
- VTS: Volume Target Spontaneous (with leak)
- C-FLOW: Continuous Flow

The C-Flow mode is type of high-flow therapy that involves the delivery of a continuous regulated flow rate (up to 60 L/min) with the possibility of an oxygen fraction (inspired fraction of oxygen (FiO_2) from 21% to 84% depending on the set oxygen supply flow rate). The gas mixture is then heated and humidified by an external humidifier and delivered to the patient through a nasal cannula.

The EO 150 ventilator can be used with three different power sources:

- Mains power;
- Internal battery;
- External DC power supply (e.g., car 12V power outlet).

The internal battery of the EOVE ventilator allows your ventilator to operate even when mains power is disrupted or when the device is not connected to the mains. When the EOVE ventilator is operating on internal battery power, you are notified of the level of charge of the battery by the battery power source indicators both on the keyboard and touch screen.

The internal battery continues to charge when the device is connected to mains power, even when it is operating or on standby. The internal battery takes 6 hours to fully charge from empty without ventilation and 6 hours when ventilating. To preserve the internal battery from too repetitive charges occurring, the internal battery may not charge if battery level is higher than 95%. To obtain a 100% charge it could be necessary to discharge the battery below 95% before plugging back the AC power.

Internal battery run time is determined by:

- Environmental conditions (operating conditions See Technical Specifications) ;
- The condition and age of the battery ;
- The device settings ;
- The current circuit in place and unintentional leak.

For additional information on power supplies and sources see the technical file "**Dossier technique EO-150 UE 2017_745 Rev I**" and IFU manual "**100_23 revDE : user manual_EO-150**".

3.2.3 Classification

The principal characteristics of the **EO-150 ventilator** are listed below in the following table:

*Table 24: Principal characteristics of the **EO-150 ventilator***

CATEGORY	CLASSIFICATION
Duration	Continuous or transient (depending on patient ventilation needs)
Invasive device	No
Body contact	No
Biological effect	Yes
Usage	Repeated use
Sterile	No
Active medical device	Yes
Software	Yes
Medicinal substance	No*
Biological material	No material derived from animal tissue or human blood is being incorporated
Radioactive device	The devices are not radioactive

* The **EO-150 ventilator** enables the delivery of air pressure or insufflated gas (e.g. oxygen). However, as these components are separate and supplied independently, the **EO-150 ventilator** is not considered a combined medical device.

The **EO-150 ventilator** is classified as a **Class IIb** device **according to Rule 12** (Rule in Annex VIII, Chapter 3 of MDR 2017/745):

All active devices intended to administer into the body and/or remove from the body medicinal products, body fluids or other substances are classified as Class IIa, unless the operation is carried out in a potentially dangerous manner, taking into account the nature of the substances in question, the part of the body concerned and the method of administration, in which case they are classified as Class IIb.

The **EO-150 ventilator** is a device intended to provide pressure to the patient which is a source of energy (forced airflow) transferred to the human body (where Rule 9 may apply: All active therapeutic devices intended to deliver or exchange energy are in Class IIa, unless their characteristics are such that they can deliver energy to or transfer energy with the human body in a potentially hazardous manner, taking into account the nature, density and site of application of that energy, in which case they are in Class IIb. All active devices intended to control and monitor the performance of active therapeutic devices in **Class IIb** or intended to act directly on the performance of such devices are in Class IIb).

However, under certain conditions of use (see Note below), the **EO-150 ventilator** delivers oxygen to the body which is considered to be medication. This explains the fact that the medical device meets **rule 12** for its classification. And according to Annex VIII, Chapter 2, Section 3.5: If several rules or, within one rule, several sub-rules apply to the same device because of its intended purpose, the rule or sub-rule that applies is the strictest, the device being classified in the highest class.

The device is intended for the treatment and alleviation of a disease. Medical device identified in the CND, GMDN coding lists.

*Note: In home ventilation and for the use of the **EO-150 ventilator**, oxygen is hardly used.*
*The **EO-150 ventilator** is intended for neuromuscular and ventilo-dependent patients (24/24H). These patients have relatively "healthy" lungs, but a physical handicap in terms of muscles and especially diaphragm activity and therefore do not require oxygenation in 90% of all cases).*
The remaining 10% of patients have COPD with a degeneration of their respiratory system. For these patients, a low oxygen enrichment is prescribed to improve gas exchange: the oxygen level is increased from 21% (air) to 30% - 40% maximum.
Indeed, it is very complicated to use and have oxygen at home, except with oxygen concentrators that deliver a low flow of 2 to 5 L/min.
*In fact, high concentration oxygen (40-100%) is used with critical care ventilators and or emergency ventilators in the hospital setting (which is not the case with the **EO-150 ventilator**).*
It is under these conditions that patients with acute respiratory attacks (resuscitation) or patients with severe trauma (e.g. road accidents) are treated.

3.2.4 Medical device therapeutic positioning

EOVE **EO-150 ventilator** is designed to treat adult and paediatric patients weighing at least 3.5kg (8lbs). They can require continuous or intermittent MV by either invasive or noninvasive approaches.

3.3 DEVICE HISTORY

The complete description of device history is found in the technical file "**Dossier technique EO-150 UE 2017_745 Rev I**", sections II- 10 and 11.

3.3.1 Predecessor devices

There is no previous generation of the **EO-150 ventilator**.

3.3.2 Design changes

The **EO-150 ventilator** is CE-marked since 15/06/2015 (notified body LNE/GMED).
Since it was launched, the changes to the medical device presented to the notified body during the audits are as follows:

*Table 25: Table of **EO-150 ventilator** notified changes*

Reference	Origin	Date of closure	Object
MOD15-001	Quality	05/04/2016	Selection and qualification of the supplier *Martin Technologie* for the manufacturing of the EOVEOne keyboard
MOD15-002	Research department, M&V	18/12/2015	Modification of the ventilation software and interface MPP mode, addition of settings for the following modes: - (A)PCV: Pressure assisted/Controlled Ventilation - PAC: Pressure Assisted/ Controlled - PSV: Pressure Support Ventilation - PSV-VT: Pressure Support Ventilation Volume regulated - ST: Spontaneous Timed - VTS: Volume Target Spontaneous Modification of the power supply software: battery pack management
MOD15-003	Research department, M&V	10/10/2016	Modification of the Clinical Data software
MOD15-004	Quality/Tech	05/04/2016	Selection and qualification of the CMPC supplier for the manufacturing of the machined block - pneumatic base (double source)
MOD15-005	Research department, Tech	06/03/2017	ASUS Zenpad Z370C-1A010A tablet replaced the ME176CX ASUS memo Pad7 tablet in obsolescence.
MOD16-001	Research department, M&V	22/09/2017	C-FLOW & proximal free mode
MOD16-002	Quality/Tech	30/11/2016	Optimisation Electrovane Staiger
MOD16-004	Research department	09/01/2017	Hamilton flow sensor
MOD17-001	M&V	02/03/2018	Pressure 80 hPa according to ISO 80601-2-72 (Canada)
MOD17-002	Research department	25/09/2018	CPU board
MOD17-003	Research department	06/03/2018	ASUS Z380M tablet
MOD18-001	Quality	06/08/2018	Selection and qualification of the supplier Inovelec for the wiring of the CPU boards
MOD18-003	Quality	25/09/2018	Frns Eolane closure Vailhauques selection St Agrève
MOD18-004	Research department	29/05/2020	Design of display and touch screen / current tablet
MOD18-005	Research department	08/01/2019	Pressure 80 hPa according to ISO 80601-2-72

Reference	Origin	Date of closure	Object
MOD19-001	Quality	24/07/2020	Battery VLAD EOVE3
MOD19-002	M&V	06/03/2020	Use of a trolley with EO-150
MOD20-001	Research department	25/09/2020	Tablet battery replacement by hardware function for the after sales service
MOD20-002	Research department	29/05/2020	Removal of O_2 valve
MOD20-003	M&V	27/05/2021	New expiratory valve version 2
MOD20-004	Quality	21/05/2021	Liquidation WACC, transfer activity S/T Mecagil-Lebon
MOD20-008	Quality	In progress	Transfer of OCP moulds to EFFIPLAST or Boursier Sogreg

There are currently no further design modifications not yet notified. There is no notification to GMED, changes are presented to GMED during annual audits.

3.3.3 Market data

Market data is found in the file "**100_612 E - Rapport annuel de sécurité - PSUR EO-150**".

Sales volume on the 31st December 2021 is 7778 **EO-150 ventilator**s in total (90% of sales are in Europe).
The EU countries in which the device is sold are:

- France
- Germany
- Austria
- Belgium
- Spain
- Ireland
- Italy
- Holland
- Portugal
- Poland
- Czech republic

3.4 CLINICAL EVALUATION PLAN

The CEP is provided in the file "**100_66 rev H : CEP_EO-150**".

3.5 CHANGES SINCE THE LAST REPORT

The last CER was completely rewritten (according to the GMED CER template and MEDDEV 2.7/1 REV 4 requirements) and submitted by EOVE to the GMED for MDR certification. This report is an update of the last certified version as all relevant materials have been updated according to the recommendations made in the previous version. The writing and update of the CER was outsourced to EFOR Group.

Since the last version (version G of the Clinical Evaluation Report) submitted to the GMED on 02 September 2022, EOVE has updated and revised a number of key elements of the Technical File. These documents were included in the version (version H) of the CER. The modifications made in the present version are listed below:

- Update of the scope of the CER: inclusion of additional details on device precautions, instruction for use, warnings, etc., see sections 2.3 – 3.1. – 3.2. (new version of the IFU file "**manual_eove_150_en_US revDE**" and technical file "**Dossier technique EO-150 UE 2017_745 Rev I**").

- An update of the applicable standards and guidance listing, see section 3.6.
- Inclusion and evaluation of a new version of the risk analysis (document reference: "**100_17 AI Risk Analysis**", excel and word file, "**100_67 - rev I - Risk management report**", "**100_15 - E - EO 150 Risk management plan**" and "**100_67 - rev I - Risk management report**"), see section 6.2.
- More detailed account of PMS and materiovigilance data, see section 6 (updated Post market surveillance plan and report : "**100_611 B - Plan de surveillance après commercialisation - EO-150**" and "**100_612 E - Rapport annuel de sécurité - PSUR - PMS EO-150**").
- Addition of usability formative tests data carried out by the manufacturer within the PMS section (see section 6.4.).
- GSPR conclusions adapted according to the changes made by the manufacturer since the last report (section 8).
- Conclusions regarding compliance with GSPRs, compliance of information materials and residual risks have all been updated to better reflect the changes made by the manufacturer since the last report.
- Additional details regarding preclinical data provided and biocompatibility tests updated in order to better justify GSPR conformity performance report, alarm and acoustic testing (see section 10.1.5.).

The current version (version I) takes in account the corrections of the GMED report RDM- CEAR EOVE P603936_P2 : NC F/06 ; NC C/11

§ 3.7.3 Claims regarding patient benefits

The **EO-150 ventilator** has no direct clinical benefit. The clinical benefit to the patient is related to the medical gas/air blend delivered to the patient - *i.e*. the ventilation therapy that is applied. As the ventilator assists in the mechanical delivery of ventilation therapy, the ventilator has an indirect patient benefit.

§ *3.10.4.7 Patient benefits*

No direct patient benefits associated only to the ventilator were described in the literature. Indeed, the benefits reported relate to the ventilation therapy – *i.e.* the gas/air blend delivered to the patient in association with the ventilator.

Nonetheless, the larger picture is that HMV has patient benefits that are applicable to the whole system and mentioned here to contextualise to how HMV benefits patients when compared to hospital ventilation:

§ *8.3 Summary of conformity assessment on acceptable benefit/ risk ratio*

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§ *8.3.3 Patient benefits*

The **EO-150 ventilator** has no direct clinical benefit. The clinical benefit to the patient is related to the medical gas/air blend delivered to the patient - *i.e*. the ventilation therapy that is applied. As the ventilator assists in the mechanical delivery of ventilation therapy, the ventilator has an indirect patient benefit.

The use of MV to treat respiratory failure has been described since the 1960s. This well-established and managed treatment is now transposable to a home setting with no damaging effect to the patients' health. This explains why HMV is now recommended by guidelines to treat the most common diseases needing MV such as COPD (COPD Working Group 2012; Ergan et al. 2019; HAS, COPD care guideline 2019), NMDs (HAS, recommendations for HMV in NMDs 2006) and OHS (NICE Guideline for OSAHS and OHS 2021). HMV has important benefits to the patient, including improved $PtCO_2$, $PaCO_2$ levels, QoL, improved respiratory compliance and lowers costs, needs for IV as well as exacerbation frequency for COPD patients. **However, this benefit is indirectly attributed to the ventilator and directly associated with the air or medical gas/air blend provided to the patient.**
All selected papers from the State of the Art unanimously state that HMV further benefits the patient compared to those treated with MV in hospitals. Adverse events reported for HMV (discomfort, oro-nasal dryness, skin lesions, dyspnoea and claustrophobia) are well known, manageable and largely outweighed by the benefits to

the patient see section 3.10.4.9. for the full list). In all the indications included, patients' life quality and expectancy are substantially reduced when MV is refused. The benefit-risk balance is entirely in favour of HMV for the treatment of respiratory failure.

3.6 STANDARDS AND GUIDANCE

For the complete history of normative developments concerning this medical device please refer to the previous versions of the technical file under CE 93/42. The main normative developments are: IEC 60601-1 Am. 2020 ; IEC60601-1-6 Am. 2020 ; IEC60601-1-11 Am. 2020 ; ISO 14971 : 2019 + A11 2021 ; ISO 80601-2-72 : 2015 ; IEC 62133-2 : 2017.

Conformity assessments for the medical device is performed according to ANNEX IX of MDR 2017/745, see documents "**100_615 Rev A"** and **" ANNEXES OBLIGATOIRES - 4 - liste des normes et documents appliqués - EO-150**".
Conformity assessments for the medical device is performed according to ANNEX I of MDR 2017/745, see the file "**100_613 rev F - Conformité à l'annexe I du règlement 2017-745**".
Product software: Apply IEC 62304: 2006 + A1 2015: see report "**100_72 Rev C Conformity to the standard IEC 62304: 2006 + A1 2015**".

The **EO-150 ventilator** meets the following standards (see file "**100_64 – Rev F - Rapport de validation normatif**"):

*Table 26: Normative requirements for **EO-150 ventilator***

Normative requirements	Document reference	Not applicable (NA)	OK
European Directive 93/42, consolidated by European Directive 2007/47.	Document 100_75 rev F (Annex I) Technical file CE rev P of 02/09/22	-	OK
EU Regulation 2017/745.	Document 100_613 rev F (annex I) Technical file EU rev I of 13/10/22	-	OK
EU Regulation UE 2021/2226 – 14/12/2021 on electronic instructions for use of medical devices	Document of compliance with regulation 100-877 rev A	-	OK
European Directive 2006/42	Document of compliance with regulation 100_44 rev B	-	OK
Directive 2011_65_EU - 8 June 2011 - ROHS2	S/T Business Case: VLAD FAB100-121 rev I INOVELEC FAB100-100 rev K	-	OK
Directive 2014_53_EU - 16 April 2014 - RED	ETSI report EN 300 328 V2.1.1: 162649-740085-A of 26 Nov 2019	-	OK
Directive 2012_19_EU - 4/07/2012 WEEE	Document of compliance with regulation 100_91 revA	-	OK
SOR/ 98-282 (Canada)	Document of compliance with regulation 100_98 revA	-	OK
RESOLUTION - RDC No. 16 March 28, 2013 (Brazil). Chapter 4: Design Control and DMR	MDSAP audit reports n° P601541_P1_20/10/2020 ; P604456_P1 _14/02/2022 Document 100-347 revA	-	OK
Directive 2006-66-EC Battery and accumulator: 2006	Subcontractor's business file VLAD document FAB100-121 rev I	-	OK
ISO 14971: 2019 / A11 : 2021	Compliance Document 100_71 rev C	-	OK

IEC 60601-1: 2012 / A2 : 2020 : Medical electrical equipment - Part 1: General requirements for basic safety and essential performance.	Report IEC 60601-1: 13334266-775156-A of 31/08/2022	-	OK
Canadian Deviations **CAN/CSA-C22.2 No. 60601-1-14:** 2014 Medical electrical equipment - Part 1: General requirements for basic safety and essential performance.	Report IEC 60601-1: 13334266-775156-A of 31/08/2022	-	OK
IEC 62304 / A1 2015 Medical device software - Software life cycle processes.	Report 100_72 C - Conformity to the standard IEC 62304 of 12/08/2022	-	OK
IEC 60601-1-2: 2014: Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral standard: Electromagnetic compatibility - Requirements and tests.	Report IEC 60601-1-2: 12967369 -773197 of 24/08/2022	-	OK
IEC 60601-1-2 / A1 2020: Medical electrical equipment - Part -2: General requirements for basic safety and essential performance - Collateral standard: Electromagnetic disturbances - Requirements and tests	Document Impact Analysis IEC 60601-1-x A1 2020 - 01 July 2021. Application not mandatory.	NA	-
IEC 60601-1-6 2010 / A1 2013 / A2 2020: Medical electrical equipment - Part 1-6: General requirements for basic safety and essential performance - Collateral standard - Suitability for use	Report IEC 60601-1-6 13334266-775156-B of 31/08/2022	-	OK
IEC 60601-1-8 2006 / A1 2012: Medical electrical equipment - Part 1-8: General requirements for basic safety and essential performance - Collateral standard: General requirements, tests and guidance for alarm systems in medical electrical equipment and systems.	Report IEC 60601-1-8: 162649-740083-C dated 20 March 2020	-	OK
IEC 60601-1-8 / A2: 2020: Medical electrical equipment - Part 1-8: General requirements for basic safety and essential performance - Collateral standard: General requirements, tests and guidance for alarm systems in medical electrical equipment and systems.	Document Impact Analysis IEC 60601-1-x A1 2020 - 01 July 2021. Non-mandatory application.	NA	-
ISO 80601-2-72 2015: Medical electrical equipment - Part 2-72: Particular requirements for basic safety and essential performance of ventilators used in the home care environment for ventilo-dependent patients.	Report ISO 80601-2-72 - 13334266-775156-D of 31/08/2022	-	OK
IEC 62366-1: 2015 / A1 2020 : Medical devices - Application of usability engineering to medical devices.	Compliance document 100_74 revE	-	OK
IEC 62133-2: 2017: Alkaline and other non-acid electrolyte storage batteries - Safety requirements for sealed portable storage batteries, and for batteries made from them, intended for use in portable applications. Part 2: Lithium systems	Report IEC 62133-2 166234-748670 B-V2 of 29 May 2020	-	OK
IEC 60601-1-11 2015 / A1 2020 : Medical electrical equipment -- Part 1-11: General requirements for basic safety and essential performance -- Collateral standard: Requirements for medical electrical equipment and medical electrical systems used in the home care environment.	Report IEC 60601-1-11: 13334266-775156-C of 31/08/2022	-	OK
IEC 60601-1-9 2007 / A1 2013: Medical electrical equipment - Part 1-9: General requirements for basic safety and essential performance - Collateral standard: Requirements for environmentally responsible design.	Report IEC 60601-1-9: 169649-742412 dated 18 March 2020	-	OK

Only for INMETRO registration (Brazil)			
ETSI EN 300-328 V2.1.1: Electromagnetic Compatibility and Radio Spectrum Matters.	Report ETSI EN 300 328 V2.1.1: 162649-740085-A dated 26 Nov 2019	-	OK
RTCA DO-160 G: Environmental Conditions and Test Procedures for Airborn Equipment. **Section 21** (Radio Frequency Energy Emission)	RTCA DO 160 G EMC Report: 162649-740094 dated 7 Oct 2019 + mechanical report n°162649-740093 dated 13 oct 2022	-	OK
ISO 15223-1: 2017 Medical devices - Symbols for use with labels, labelling and information to be provided for medical devices - Part 1: General requirements	Document 100_65 C "Functional verification report	-	OK
The sign  defined by the standard **EN 50419** (*Marking of Electrical and electronic equipment: 2005*) shall be affixed to the ventilator.	Document 100_65 C "Functional verification report	-	OK
ISO 10993-1 : 2018 :« Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process»	Document 100_69 C (p) "Biocompatibility evaluation plan" + Document 100_69 C (r) "Biocompatibility evaluation report"		OK
ISO 18562-1: 2017 Biocompatibility evaluation of breathing gas pathways in healthcare applications – Part 1: Evaluation and testing within a risk management process.	Document 100_69 C (p) "Biocompatibility evaluation plan"+ Document 100_69 C (r) "Biocompatibility evaluation report"+ external report ISO 18562-1 - Risk Assessment EO-150 n°1001565584-4974254BA - 27 sept 2022		OK
ISO 18652-2 : 2017 Biocompatibility evaluation of breathing gas pathways in healthcare applications – Part 2: Tests for emissions of particulate matter	ISO18652-2 report n° 1001600886-5077340P R1 of 29/08/2022		OK
ISO 18652-3 : 2017 Biocompatibility evaluation of breathing gas pathways in healthcare applications – Part 3: Tests for emissions of volatile organic compounds (VOCs)	ISO18652-3 report n°1001565584-4974254 of 25/08/2022		OK

3.7 CLAIMS OF TECHNICAL PERFORMANCE, CLINICAL PERFORMANCE/BENEFIT AND SAFETY

3.7.1 Technical performances intended by the manufacturer

The technical performances claimed by EOVE for the **EO-150 ventilator** are the following:

- Compliant with performance standards : ISO 80601-2-72:2015
- Ensure an airflow between 1 and 60 L/min
- Ensure a volume between 30ml to 2.5 L
- Ensure a set insufflation pressure between 5 and 49 mb
- Ensure a set exhalation pressure between 1 and 25 mb
- Ensure a minimum breath rate of 5 to 80 c/min
  To set off appropriate alarms according to ISO 80601-2-72:2015 (specified in section 10.1.5.2.)

3.7.2 Clinical performances intended by the manufacturer

The manufacturer of the device under evaluation, **EO-150 ventilator**, does not claim any clinical performances.

3.7.3 Claims regarding patient benefits

The **EO-150 ventilator** has no direct clinical benefit. The clinical benefit to the patient is related to the medical gas/air blend delivered to the patient - *i.e*. the ventilation therapy that is applied. As the ventilator assists in the mechanical delivery of ventilation therapy, the ventilator has an indirect patient benefit.

3.7.4 Claims regarding clinical safety

The clinical safety claims for the medical device **EO-150 ventilator** are:

- safe for adults and children (over 3.5kg) ;
- suitable for use in hospitals, medical centres or at home ;
- deployment of a backup ventilation module in case of failure.

3.8 DEVICE PRESUMED TO BE EQUIVALENT

Not applicable. Equivalence will not be used to prove the performance and safety of the **EO-150 ventilator.**

3.9 DEVICE UNDER EVALUATION

3.9.1 Demonstration of equivalence (only when equivalence is claimed)

Not applicable. Equivalence will not be used to prove the performance and safety of the devices.

3.9.2 Equivalent device description: Clinical, technical, biological

Not applicable. Equivalence will not be used to prove the performance and safety of the devices.

3.9.3 Clinical equivalence: Discussion about similarities and differences

Not applicable. Equivalence will not be used to prove the performance and safety of the devices.

3.9.4 Technical equivalence: Discussion about similarities and differences

Not applicable. Equivalence will not be used to prove the performance and safety of the devices.

3.9.5 Biological equivalence: Discussion about similarities and differences

Not applicable. Equivalence will not be used to prove the performance and safety of the devices.
Furthermore, the biological equivalence is not required because **EO-150 ventilator** device meets gas pathway biocompatibility as disclosed in test report "**100_69 Rev C - Biocompatibilty evaluation report EO150".**

3.9.6 Equivalence of instruments

Not applicable. Equivalence will not be used to prove the performance and safety of the devices.

3.9.7 Conclusion concerning equivalence

Not applicable. Equivalence will not be used to prove the performance and safety of the devices.

3.9.8 Data access

Not applicable. Equivalence will not be used to prove the performance and safety of the devices.

3.10 CLINICAL BACKGROUND, CURRENT KNOWLEDGE, STATE OF THE ART

3.10.1 Medical fields

This part of the CER on the **EO-150 ventilator** addresses the State of the Art and clinical knowledge.

The aim of this part is to better understand the clinical context associated with the use of the devices and to take stock of the State of the Art in the medical field to which the products relates.

This part dedicated to the State of the Art and clinical knowledge will focus on discussing the place and interest of the **EO-150 ventilator** for the treatment of respiratory insufficiency at home.

3.10.2 Data from the literature

As requested in MEDDEV 2.7 / 1 Rev. 4, this Clinical Evaluation is based on a defined and methodologically sound process based on a critical review of the currently available scientific and medical literature.

The detailed protocol "Literature search protocol" is available in APPENDIX 4: STATE OF THE ART - LITERATURE SEARCH in this CER and in the electronic appendix: "**100_66 rev G : EO-150_literature_search_protocol"**. The associated results "Literature search report" are available in APPENDIX 5: STATE OF THE ART - LITERATURE SELECTION in this CER and in the electronic appendix: "**100_66 rev G** : **EO-150_literature_search_report"**.

The protocol has been followed with no deviation. Inclusion and exclusion criteria have been met, and no selection criteria are intended to procure only favourable or unfavourable criteria. Thus, both favourable and unfavourable data were considered in the search protocol.

3.10.2.1 National registries

No national registry was identified in this CER.

3.10.2.2 Guidelines and recommendations

The results of the search are included in the file "**100_66 rev G** : **EO-150_literature_search_report".**

3.10.3 Clinical data

The results of the search are included in the file "**100_66 rev G** : **EO-150_literature_search_report".**

3.10.3.1 Other collected data

The results of the search are included in the file "**100_66 rev G : EO-150_literature_search_report".**

3.10.3.2 Results of the literature search

The identification and selection of relevant data sets is summarised in the APPENDIX 5: STATE OF THE ART - LITERATURE SELECTION. Of the initial 356 data sets found, 195 data sets were selected based on relevant titles and abstracts. Conversely, 161 data sets were excluded. Subsequent review of the full text articles enabled exclusion of 67 additional data sets. 2 manual search results were included. As a result, 130 data sets (16 guidelines, 112 articles and 0 vigilance data) were included in the State of the Art and clinical knowledge part of this CER.

The list of identified and included/excluded items with reasons for exclusion is detailed in the file "**100_66 rev G : EO-150_literature_search_report"**.

3.10.4 State of the Art

The literature and investigations underline the performance of home mechanical ventilators in the context of artificial ventilation. Findings demonstrate the impact of this technology on patient health and wellbeing.

3.10.4.1 Respiratory disorders

The following State of the Art will focus on describing the pathologies or medical situations where treatment by MV is indicated, such as COPD, OHS, NMDs and others.
This part of the State of the Art includes:

- A description of the normal evolution and consequences of the medical conditions concerned, if there are different clinical forms, steps and severity and the occurrence in the population;
- A description of the available therapeutic solutions with their advantages and disadvantages;
- A description of benefits, risks and undesirable side-effects.

Respiratory insufficiency can be caused by many different conditions but there are two main types of respiratory failures: hypoxemic respiratory failure (type I) or hypercapnic respiratory failure (type II). Type I respiratory failure is characterised by lower arterial oxygen tension (PaO_2 < 60mmHg or 8.0 kPa) and low or normal arterial carbon dioxide tension ($PaCO_2$ <50 mmHg or 6.0 kPa). It is associated with most acute lung diseases such as: low ambient oxygen (e.g. high altitude), ventilation-perfusion mismatch (e.g. pulmonary embolism), alveolar hypoventilation (e.g. acute NMDs), diffusion problem (e.g. pneumonia) or shunt (e.g. oxygenated and non-oxygenated blood mixing). Type II respiratory failure is defined by a high $PaCO_2$ (> 50 mmHg or 6.0 kPa), also known as hypercapnia, caused by a build-up of carbon dioxide as alveolar ventilation is insufficient to expel the excess carbon dioxide. Common disorders associated to hypercapnia are NMDs, chest wall abnormalities (e.g. deformation, rigidity or flail chest), increased airway resistance (e.g. asthma or COPD), reduced breathing effort (e.g. OHS or drug overdose) and decreased lung area available for gas exchange (e.g. chronic bronchitis).

3.10.4.1.1 Chronic Obstructive Pulmonary Disease (COPD)

Definition
Chronic obstructive pulmonary disease, also known as COPD, includes multiple lung conditions that cause breathing difficulties. According to the world health organisation (WHO), it is the third leading cause of death worldwide, having caused around 3.23 million deaths in 2019. It is mostly caused by inhalation of harmful fumes or dust (e.g. tobacco smoke, air pollution, chemicals etc.), asthma, but can also be the result of a rare genetic problem (alpha-1-antitrypsin deficiency, AAt) leaving the lungs more susceptible to damage (Koblizek et al. 2013). This condition mostly affects middle-aged or older adults who smoke. The two main characteristics of COPD are emphysema, damage to the lung air sacs, and chronic bronchitis which is a long term inflammation of the airways. COPD symptoms are typically breathlessness, persistent chesty cough, frequent chest infections, chest tightness, persistent wheezing, lack of energy and/or phlegm production.
Symptoms only progressively worsen if left untreated and can also lead to more frequent acute phases of respiratory failures called flare-ups or exacerbations marked by dyspnoea, cough and sputum production (Wedzicha et al. 2017). These episodes can last for several days and significantly hinder the patients' QoL and shorten their lifespan (van Hirtum et al. 2018).

Diagnosis
No single test or symptom allows healthcare professionals to diagnose COPD. Diagnosis is often carried out after establishing the patients' breathing-related symptoms, smoking history, family history of lung disease, lung function, body mass index (BMI), a chest examination, a spirometry test and a blood test to rule out other disorders. Other tests can be carried out to confirm the COPD diagnosis such as an electrocardiogram (ECG), echocardiogram, a peak flow test, a CT scan and a phlegm sample (HAS, COPD care guideline 2019; Koblizek et al. 2013).

Treatment

Although there is no cure for COPD, standard care mostly involves treating the symptoms to help slow down disease progression and prevent phases of exacerbation (HAS, COPD care guideline 2019; Koblizek et al. 2013). Major lifestyle changes are firstly recommended:

- Stop smoking ;
- Practice regular exercise and improve diet ;
- Vaccination against pneumonia, influenza and coronavirus ;
- Specialised pulmonary rehabilitation.

Then, to relieve symptoms and limit flare ups, medication is offered depending on the stage of COPD (Wedzicha et al. 2017):

- Short acting bronchodilator inhalers (beta-2 agonists or antimuscarinic): relax and widen airways – first line of treatment for occasional breathlessness ;
- Long- acting bronchodilator inhalers (beta-2 agonists or antimuscarinic): for more persistent symptoms
- Steroid inhalers: to reduce airway inflammation, usually in combination with long-lasting inhalers (Wedzicha et al. 2017) ;
- Theophylline tablets: bronchodilator that reduces airway inflammation and relaxes the lining muscles ;
- Mucolytics: thins the phlegm built up in the throat making it easier to cough up ;
- Steroids: can be prescribed if the patient is suffering from severe exacerbation to reduce airway inflammation ;
- Antibiotics: in case of chest infection.

Other treatments available for more severe COPD are:

- Non-invasive positive pressure ventilation (NIPPV): supports the lungs by applying positive pressure via a mask or nasal cannula. Often administered after severe exacerbation (Budweiser, Jörres, et Pfeifer 2008; COPD Working Group 2012; X. He et al. 2021a; Osadnik et al. 2017; Sinuff, Keenan, et Department of Medicine, McMaster University 2004) ;
- Long-term oxygen therapy (LTOT): usually through HMV, is considered an option once the patient's COPD is stable. Stops hypoxemia from decreasing too much. Advised use for at least 16 hours a day (Macrea et al. 2020; Raveling et al. 2021) ;
- Surgery: only applies to a small number of people whose symptoms cannot be controlled with medicine as they present significant risks. Three possible surgeries available: bullectomy, lung volume reduction surgery or a lung transplant.

Complications

The following common complications can occur in patients with COPD:

- Respiratory infections ;
- Sleep apnoea ;
- Heart problems: atrial fibrillation (AFib) ;
- Lung cancer ;
- High blood pressure in lung arteries ;
- Depression and anxiety.

3.10.4.1.2 Obesity Hypoventilation Syndrome (OHS)

Definition

Today around 1 in 3 adults worldwide is overweight (BMI ≥ 25k g/m²) and 1 in 10 are in fact obese (BMI ≥30 kg/m²). Obesity is now considered an epidemic, and with it an increase of the many comorbidities associated to obesity, notably obesity hypoventilation syndrome(OHS), have been reported (Soghier et al. 2019). This condition is also known as Pickwickian Syndrome which comes from a character in the Charles Dickens novel *'The posthumous Papers of the Pickwick Club'* who presented with similar symptoms. OHS is described as a chronic diurnal alveolar hypoventilation with a high daytime PCO_2 (> 45 mmHg) and low oxygen levels.

OHS is often associated to obstructive sleep apnoea (OSA) which involves periods of reduced or absent breathing during sleep. But OHS differs from OSA in that patients exhibit longer periods of night-time hypoventilation and

daytime hypercapnia (NICE Guideline for OSAHS and OHS 2021). Hence, OHS symptoms are often the result of poor sleep and poor oxygen levels, which can manifest themselves in several forms including tiredness, lack of energy, breathlessness, headaches and depression.

There does not seem to be a single cause for OHS but rather an accumulation of factors, including obesity, that result in hypoventilation. It is thought that the excess of fat-producing hormones, such as leptin, negatively impact breathing. Leptin resistance seems to reduce the surface tension of lung tissue which weakens ventilation responsiveness and causes hypercapnia. Moreover, the excess fat and its distribution mean it can be physically challenging for the lungs to function correctly and upper airways are obstructed (de Lucas-Ramos et al. 2004).

Diagnosis

The OHS diagnosis cannot be established on patient history and symptoms alone. The two main indicators that confirm the diagnosis are (Mokhlesi et al. 2019; NICE Guideline for OSAHS and OHS 2021):

- BMI ≥ 30kg/m²
- Diurnal hypoxemia and daytime hypercapnia: arterial measure of capillary blood gases

Other investigatory tests can help better define the severity of OHS and rule out other respiratory disorders (Mokhlesi et al. 2019):

- Chest X-ray or CT scan: sign of chest wall deformities or cardiomegaly ;
- Echocardiogram: may show right ventricular hypertrophy linked to severe lung disease ;
- ECG: heart arrhythmias ;
- Pulmonary function tests (PFTs): (i) flow volume loop to determine if there is upper airway obstruction and (ii) reduction of forced vital capacity (FVC) and expiratory reserve volume ;
- Sleep study: an overnight polysomnograph to confirm sleep hypoventilation, hypoxia and hypercapnia.

Treatment

NICE guidelines (NICE Guideline for OSAHS and OHS 2021)

Lifestyle changes are firstly recommended:

- Lose weight: weight-loss alone can often help reverse most of the OHS-related symptoms although patients are often refractory to long term dietary changes ;
- Reduce or avoid smoking and alcohol consumption ;
- Regular physical exercise ;
- Good sleeping habits ;
- Bariatric surgery: to help with weight loss (e.g. gastric bypass, sleeve gastrectomy, etc.).

But other treatments help with breathing issues that commonly occur during sleep for OHS patients (Mokhlesi et al. 2019):

- MV using either CPAP or bilevel positive airway pressure (BiPAP or BPAP) to relieve upper airway obstruction, increase alveolar ventilation and help with the clearance of accumulated carbon dioxide ;
- Oxygen therapy if hypoxemia persists with noninvasive ventilation (NIV) ;
- IV via tracheostomy in cases of severe acute ventilatory failure.

Complications

The most common complication are associated with heart conditions as OHS puts pressure on the heart. Hence, OHS patients often suffer from:

- Hypertension: high blood pressure ;
- Cor pulmonale: alteration of right ventricle structure and function ;
- Angina: reduced blood flow to the heart, a warning sign of increased risk of stroke ;
- Pulmonary hypertension: high blood pressure in the lungs.

Moreover, as OHS is often associated to OSA, other typical complications are linked to poor sleep quality:

- Tiredness ;
- Lack of energy ;

- Depression, irritability.

3.10.4.1.3 Respiratory insufficiencies in Neuromuscular Disorders (NMD)

Definition

Neuromuscular disorders is a broad term for a group of inherited rare genetic diseases that involve muscle impairment either directly or indirectly via a nerve pathology. Two main groups have been determined depending on the progression rate:

- Rapid progression NMD: patients with such disorders see their life expectancy considerably shortened and the severity of muscle impairment worsen quickly over a few months (e.g. Duchenne muscular dystrophy (DMD) (HAS, DMD guidelines 2019) and amyotrophic lateral sclerosis (ALS) (HAS, ALS care guideline 2006; 2007)).
- Slowly or variable progression NMD: life expectancy is not so reduced and muscle weakening occurs over years (e.g. limb girdle, facioscapulohumeral, myotonic muscular dystrophy and Becker's muscular dystrophy (HAS, Becker's muscular dystrophy care guideline 2019)).

Although each NMD is rare, an estimated 500,000 people in Europe are effected. There are a wide variety of symptoms reported in NMDs including alteration of sensation, pain, muscle weakness, fatigue, heart and breathing issues. Initially, most NMD patients do not present with respiratory symptoms even though the large majority do not have normal respiratory function. Indeed, the main cause of respiratory insufficiency in patients with NMDs is respiratory muscle weakness. This respiratory failure can become chronic and increasingly severe in more advanced stages at which point the conditions becomes life-threatening.

Diagnosis

Diagnosis of NMDs can vary depending on the individual disease but overall, NMDs can be diagnosed by establishing patient symptom history and the following tests (HAS, ALS care guideline 2006; NICE, NMD management guideline 2019):

- Family health history and genetic testing: if suspected NMD is hereditary ;
- Electromyography: test muscle and nerve electrical activity at rest ;
- Blood tests: to eliminate possibility of inflammation and measure levels of various chemicals and/or antigens that are associated to the suspected NMD (e.g. increase in muscular enzymes creatine kinase);
- Muscle biopsy histological assessment can help with diagnosis and defining disease stage.

Although not always initially present, some symptoms are a sign that the patients' respiratory function is deteriorating and respiratory muscles are weakening (NICE, NMD management guideline 2019):

- Dyspnoea or shortness of breath following physical effort and/or at rest ;
- Orthopnoea or breathlessness when lying down ;
- Insomnia and frequent sleep disruption ;
- Morning headaches ;
- Dysphagia or difficulty swallowing ;
- Loss of appetite ;
- Excessive sleepiness during the day ;
- Depression and/or anxiety ;
- Increase in diurnal levels of blood carbon dioxide ($PaCO_2$ > 6 kPa) ;
- Rapid decompensation in ventilatory function.

Treatment

As there is today no cure for NMDs, treatment revolves mostly around symptom management (HAS, invasive ventilation in NMDs 2020; HAS, recommendations for HMV in NMDs 2006; NICE, NMD management guideline 2019). Respiratory insufficiency in progressive NMD requires assisted ventilation, without this, the patient's prognosis is extremely poor. As the disease worsens, ventilation dependency increases and ventilator settings must follow suit. Standard care is NIV to aid respiratory muscles improve gas exchange and correct alveolar hypoventilation. This line of treatment considerably improves patients' lifespan and is the most effective treatment to date for NMD patients (E. I. Schwarz et Bloch 2019; Wolfram Windisch et al. 2018).

Complications

Complications of NMDs differ from one disorder to another, but overall the degradation of muscle function reaches critical levels for respiratory muscles, meaning the patient needs life-supporting ventilation at late-stage NMD. Thus, difficulties encountered in NMDs depend mostly on the stage of advancement and are linked to muscular weakening which manifests as a lack of proper breathing function (symptoms above-mentioned in the section *diagnosis*).

3.10.4.1.4 Respiratory insufficiencies linked to chest wall malformation

Definition

The chest wall is composed of bone structures (ribs and spine), respiratory muscles and nerves connecting these muscles to the central nervous system. Structural abnormalities can lead to various health problems ranging from mild to severe. The chest wall is critical for the respiratory diaphragmatic pump, which is the structure that provokes bulk transfer of air to and from the alveoli which allows the expansion and contraction of the lungs. Thus, thoracic malformations can be linked to restrictive respiratory physiology associated to long term hypercapnic respiratory failure (Wolfram Windisch et al. 2018). Chest wall disorders, or restrictive thoracic disorders (RTDs), can be organised according to the structure affected:

- Spine and articulation:
  - Kyphoscoliosis: begins in early adolescence (idiopathic adolescent scoliosis) and may be genetic. Respiratory muscles can be weakened leading to a reduction in lung volume and respiratory system compliance. Long term hypoventilation means hypoxemia and hypercapnia as well as significantly impaired physical exercise capacity. It is possible to predict respiratory failure, and subsequent treatments, by measuring the Cobb angle of the kyphotic or scoliotic curves.
- Ribcage:
  - Flail chest: describes a condition in which a fragment of the ribcage is detached from the rest of the chest wall following blunt chest trauma. This disconnected segment can move during respiration phases which could hinder breathing.
  - Pectus excavatum (PE): also called *funnel chest* or *concave chest*, occurs when the breastbone, or sternum, is pushed inwards instead of being level with the ribs. This conditions affects around one in 1000 children and is four times as common in boys than in girls.
  - Pectus carinatum (PC): also called *pigeon chest*, occurs when the breastbone, or sternum, is pushed outwards instead of being level with the ribs. But other areas of the ribcage might be pushed inwards. This disorder is also more common in boys than in girls and around one in 1500 children are affected. Both pectus disorders are caused by the cartilage in the ribcage overgrowing, a genetic link is suspected. Respiratory failure occurs only in adults with the most severe forms of pectus malformation.
  - Ankylosing spondylitis: an inflammatory disease that can cause over time vertebrae to fuse. When ribs are affected deep breathing can be compromised. A genetic link to the HLA-B27 genes is suspected.

Diagnosis

Chest malformations can be diagnosed by a variety of tests but mostly scans (radiography and/or CT scan) to give a more detailed assessment of the chest anatomy. For example, assessments using the Haller index for pectus disorders measures the degree of the CWD. Moreover, breathing tests can be carried out to determine the extent of respiratory impairment.

Treatment

The treatment depends on the problems caused by the chest wall malformation. If a patient with CWD suffers from respiratory insufficiency, MV is an option (van den Biggelaar et al. 2020; E. I. Schwarz et Bloch 2019; Wolfram Windisch et al. 2018). But if the breathing impairment is severe a surgery to correct the deformity can be suggested.

Kyphoscoliosis treatment involves chest physiotherapy, bronchodilators, oxygen therapy, NIV and diuretics if needed. NIV is usually given to Kyphoscoliosis patients as nocturnal negative pressure ventilation if they are considered high-risk or as a definite therapy for respiratory failure (van den Biggelaar et al. 2020; E. I. Schwarz et Bloch 2019; Wolfram Windisch et al. 2018).

Complications

As patients presenting CWD can suffer from respiratory failure, complications linked to this impairment include limited physical effort capacities and long term hypoventilation. Other complications are linked to the use of the ventilator itself such as patient-ventilator asynchrony (PVA), induction of upper airway obstruction during sleep and patients' physical discomfort.

Complications in severe Ankylosing spondylitis might include (i) uveitis (eye inflammation), (ii) compression fractures that could lead to back pain, spinal cord or nerve damage and (iii) increased risk of cardiovascular disease (inflamed aorta).

Occurrence of pectus deformities in children and young adults often cause severe psychological problems including anxiety.

3.10.4.2 Respiratory failure management

The next section will be dedicated to describing the performance and safety of artificial ventilation. Indeed, for the device under study, home mechanical ventilators are intended to deliver air pressure and/or gas. In comparison, artificial ventilation, which is described in the following 29 articles selected, is obtained through the use of a whole system that includes the home mechanical ventilator but also tubing, masks or cannulas. The performance and safety of the home mechanical ventilator is not described on its own and cannot be extracted from the performance and safety of the whole system.

3.10.4.2.1 Introduction

Although he did not know it yet, Andreas Vesalius, a Dutch professor of anatomy published in 1543 a ground-breaking book *De Humani Corporis Fabrica Libri Septem*, in which the first ever mention of positive pressure ventilation (PPV) as we know it today, can be found. In it, he describes what is today known as invasive ventilation (IV) via tracheostomy, insertion of an endotracheal tube and application of positive pressure ventilation. As innovative as this method of mechanical ventilation was, it was set aside for centuries as the notion of negative pressure ventilation became increasingly prominent. In 1838, a Scottish doctor, John Dalziel, described a manually operated negative-pressure ventilator, in which patients were placed, except for their heads, in an air-tight box. The negative air pressure inside the chamber and around the patient would allow lungs to fill with air. The *iron lung* was presented in 1876 by Eugene Woillez which lead to a democratisation across hospitals of MV. In fact, from the 1930s to the 1960s the widespread use of the iron lung was at its peak during the world wide epidemic of poliomyelitis, where severely ill patients desperately needed artificial ventilation. Other types of negative pressure ventilation chambers then followed suit such as the *raincoat* or the *chest cuirass*, but the use of negative pressure ventilation eventually lost momentum. They are heavy, large and cumbersome devices, which offer only limited access to the patient and other issues such as excessive leaking meant that it was progressively replaced by PPV from the 1960s. Nowadays, the most commonly used type of artificial ventilation is PPV. Moreover, with NIPPV, MV could now be used intermittently and not just as life support. Pressure targeted ventilation then became the next great innovation for NIPPV as it better adapts to the patients ventilation needs (Ram et al. 2004).

3.10.4.2.2 Mechanical ventilation (MV)

NIV can be an acute therapy for patients with respiratory failure but can sometimes be more permanently needed. According to German national guidelines, if at least one of the following criteria is met it is highly

recommended to initiate long-term NIV treatment: (i) chronic daytime hypercapnia ($PaCO_2$ ≥ 50 mmHg), (ii) nocturnal hypercapnia ($PaCO_2$ ≥ 55 mmHg), (iii) mild daytime hypercapnia ($PaCO_2$ 46-50 mmHg) and an increased $PtCO_2$ (≥ 10 mmHg) during sleep, (iv) persistent hypercapnia ($PaCO_2$ ≥ 53 mmHg) 14 days following acute ventilation therapy for acute respiratory acidosis and (v) only NIV is effective for decannulation following prolonged weaning and for symptom management (De Braekeleer et Toussaint 2021; Wolfram Windisch et al. 2018).

NIPPV allows the delivery of PPV via a facial mask or tight-fitting nasal tube (Fernandez et al. 2012). This is opposed to invasive PPV which requires the placement of an endotracheal tube via a tracheostomy, a surgical incision through the neck and into the trachea (Marchese et al. 2010; Stieglitz et al. 2013). Previously, if daytime ventilation needs increased patients were placed on IV via tracheostomy, but now non-invasive MPV, full facial masks or nasal cannula are more widely used as they are more comfortable for the patient (Callegari et al. 2017; Fernandez et al. 2012; Sinuff, Keenan, et Department of Medicine, McMaster University 2004; Toussaint et al. 2021). PPV itself decreases breathing resistance, helps correct hypercapnia and improves alveolar ventilation.

The two most common pressure-control ventilation modes on NIPPV devices are:

- Continuous positive airway pressure (CPAP): assists the patient with their spontaneous inhalation with exhalation being carried out against the same pressure
- Bi-level positive airway pressure (BiPAP, PSV): different pressure settings are applied for the inhalation (Inspiratory Positive Airway Pressure, IPAP) and exhalation (Expiratory Positive Airway Pressure, EPAP). This helps patients during exhalation who struggle to overcome the pressure used for inhalation and improve patient-ventilator synchrony (Sinuff, Keenan, et Department of Medicine, McMaster University 2004).

Moreover, ventilation settings can be determined according to two parameters: the tidal volume (V_T) or the pressure. Volume-controlled ventilation (VCV) and pressure-controlled ventilation (PCV) are two different control variables within a same ventilation mode. Nevertheless, VCV has been developed to overcomes issues caused PCV such as variable tidal and minute ventilation volumes. VCV can guarantee the safety of a pre-determined effective V_T and minute ventilation but physicians are required to appropriately set the inspiratory flow and inspiratory time. This augmented pressure increases the risk of ventilation-induced injury. But PCV modes are the most commonly used for applying NIPPV as they are generally considered more comfortable than VCV modes (Sinuff, Keenan, et Department of Medicine, McMaster University 2004). So-called hybrid modes are a mix of volume- and pressure-control modes which combine the advantages of both: volume-assured pressure support (VAPS). Dual-control modes are volume-targeted and based on the patients degree of airway restriction, coordination and ability to automatically regulate inspiratory/expiratory pressure. VAPS modes seem to improve the management of long-term ventilation compared to classical ventilation modes, although more robust clinical data is needed (Rabec et al. 2016; Zhang et al. 2020a). Moreover, using high-intensity settings for NIV (HI-NIV) has highlighted the efficacy of long-term NIV in COPD patients notably. This ventilation mode aims at lowering $PaCO_2$ as much as possible in a short time by setting a clear gas exchange goal, setting a high IPAP and high backup respiratory rate (BURR) (van der Leest et Duiverman 2019).

Nowadays, NIPPV is standard care for many disorders presenting respiratory failure, whether it be an acute or a long term impairment. It has been proven effective for a number of disorders including sleep disorders, COPD (Altintas 2016; Hess 2004; Kondo et al. 2017; Liao et al. 2017; Ram et al. 2004; Raveling et al. 2021; F. M. Struik et al. 2014), OHS, ventilation impairments associated to NMDs (NICE, NMD management guideline 2019) or CWD to name a few (E. I. Schwarz et Bloch 2019; Wolfram Windisch et al. 2018).

An innovative method of oxygen therapy name high-flow nasal cannula (HFNC) therapy, also known as high-flow oxygen therapy (HFOT), is based on high-flow delivery of a heated and humidified oxygeNAir blend. This unique nasal ventilation mode of airflows of up to 60 L/min, has proven effective for patients with acute respiratory failure (Nishimura 2016). Benefits of HFNC therapy include reduced anatomical dead space, improvement of gas exchange, positive end expiratory pressure (PEEP), constant FIO_2 and good airway humidification. Evidence in adults is still scarce but first reports suggest it is most effective in acute respiratory failure, notably COPD

exacerbation and COVID-19 (NICE - COVID-19 management guideline 2022). However, clear-cut recommendations regarding indication, initiation and stopping HFNC therapy is still lacking. Zheng et al. suggested a protocol to comprehensively compare HFNC therapy to NIV in the treatment of COPD patients and acute hypercapnic respiratory failure (Zheng et al. 2021). They put forward the following outcome measures: treatment failure, arterial blood gas (ABG) analysis, dyspnoea score, comfort score, mortality rate, and length of stay in the intensive care unit (ICU) and/or hospital. As mentioned in the "*Device evaluation criteria"* section, all of these are commonly assessed in ventilation treatment studies. Moreover, as with the other types of MV, it is key to know which patients will benefit the most from these therapies. In the case of COVID-19 or pneumonia patients with AHRF, prediction of HFNC therapy failure can be strongly correlated to the ROX index and the ratio SpO_2 to RR (Prakash et al. 2021; Zhou et al. 2022).

3.10.4.2.3 Health-related quality of Life (HRQL)

A recent comprehensive review of long-term NIV in COPD by Majorski et al. highlighted that although patient health is a main goal, long-term ventilation must also focus on factors such as QoL (Majorski et al. 2021). Indeed, they highlight that advances in telemedicine have moved long-term ventilation into a home setting which seems to benefit both the patients and healthcare centres.

Indeed, tool have been developed over the last two decades to better quantify and evaluate this parameter. There are a multitude of variants of HRQL assessment questionnaires, but the most widely used is the severity respiratory insufficiency (SRI) questionnaire (Wolfram Windisch et al. 2003). This 49-question tool was developed to assess the social, psychological and physical health aspects of the patients' life by helping them give subjective answers using a five-point system. Each item covers the following topics:

- Social item:
  - quality and/or changes of social relationships ;
  - limitations in social activities ;
- Physical health item:
  - respiratory complaints ;
  - dyspnoea ;
  - sleep disturbance ;
  - other physical impairments ;
- Psychological item:
  - wellbeing ;
  - anxiety.

To increase its accuracy, a version of this questionnaire now exists for each indication but also in multiple languages (Budweiser et al. 2007; Raveling et al. 2020; Fransien M. Struik, Kerstjens, et al. 2013; Wolfram Windisch et al. 2008). Other HRQL assessment tools include the MOS 36-item short-form health survey (SF-36) (Duiverman et al. 2020; Zhang et al. 2020b), hospital anxiety and depression scale (HADS) (van den Biggelaar et al. 2020; Duiverman et al. 2020), St George's respiratory questionnaire (SGRQ) (Ergan et al. 2019; Raveling et al. 2021; Wijkstra et al. 2002; Zhang et al. 2020b) and the maugeri respiratory failure questionnaire (MRF26); the two latter are also disease-specific. In fact, HRQL assessment questionnaires have been reported as a prognostic factor and a predictor of mortality for patients with chronic respiratory failure (Carone et al. 2016).

3.10.4.2.4 Home mechanical ventilation (HMV)

As suggested above, the next section is dedicated to the performance and safety of artificial ventilation, since data applicable specifically to home mechanical ventilators cannot be separated from the whole system that includes the home mechanical ventilator, tubing, masks or cannulas. Data from the following section will be used to demonstrate the performance and safety of artificial ventilation but will not be considered for the *EO-150* device specifically.

Devices used for HMV have been identified for the following conventional ventilation modes*:*

- (A)PCV: Pressure Assisted/Controlled Ventilation (with expiration valve) ;
- MPV: Mouth Piece Ventilation (with mouthpiece) ;
- CPAP: Continuous Positive Airway Pressure (with flight) ;

- ST: Spontaneous Timed (with flight) ;
- PAC: Pressure assisted controlled (with leak) ;
- VTS: Volume Target Spontaneous (with leak).

The following devices are used for the conventional ventilation modes mentioned above:

- Monnal T40 and T50 (ALMS) ;
- VIVO 50, VIVO 60 and NIPPY3/3+ (Breas) ;
- Ventilogic LS (Lowenstein) ;
- PB 560 (Medtronic) ;
- Trilogy (Philips Respironics) ;
- Astral 100/150 and Elisee 150 (Resmed).

EXPLOR!	Air Liquide HEALTHCARE	BREAS	EOVE	LÖWENSTEIN medical	Medtronic	PHILIPS RESPIRONICS	ResMed	
Company	MONNAL T50	Nippy 3 / VIVO 50 & 60		EO 150	VENTILOGIC LS	PB 560	TRILOGY 100 / TRILOGY 200	ASTRAL 100 / ASTRAL 150	
THERAPY									
Mode	PSV PCV PCV(A) VCV VCV(A) SIMV	CPAP PSV PSV(T) PCV •	CPAP PSV PSV(T) PCV • PCV(A) • PCV(T) PCV(A+T) VCV •	CPAP PCV,PCV(A) PSV+Smart VCV,VCV(A) SIMVp, SIMVv	CPAP PSV PCV,PCV(A) VCV,VCV(A)SIMV	CPAP PSV PCV,PCV(A) VCV,VCV(A) SIMV	CPAP PSV PCV,PCV(A) VCV,VCV(A) SIMVp, SIMVv AVAPS -AE	CPAP PSV PCV,PCV(A) VCV,VCV(A) SIMVp, SIMVv iVAPS Auto (Only NIV)	
Specific Mode	BOOST Vt target		MPV Mode Vt target	MPV mode C FLOW Vt target	LIAM MPVp Mode MPVv Mode Air trap control, Volum compensation Trigger Lockout	Vt target	AVAPS-AE; MPV mode AVAPS (Adjustable) Expiratory Sensor for Trilogy 200 only	IVAPS-AUTO Vt target	
Mode Adult/Pediatric Special Configuration on Interface	✓		✓	✓				✓	✓
Manual Breath	✓				✓				✓
Sigh Breath	✓		✓			✓	✓		✓
Apnea Ventilation	✓	✓	✓	✓		✓		✓	✓
Preset Programs	2	3	3	4	3		2	2	4

*Figure 43: **EO-150 ventilator** similar devices for conventional ventilation modes*

C-Flow mode

Description

An additional ventilation setting on the **EO-150 ventilator** is the C-Flow mode that allows to deliver a continuous regulated flow rate up to 60 L/min with the possibility of an oxygen fraction (FiO_2 from 21% to 84% depending on the set oxygen supply flow rate). The gas mixture is then heated and humidified by an external humidifier and delivered to the patient through a nasal cannula.

Table 27: c-flow mode settings according to patient typology

Settings	Adult	Paediatric	Limitations
Flow (L/min)	2-60	2-60	None
Press. Max (mb)	7-50	2-60	None

Therapeutic indications

Humidified high-flow oxygen therapy has been used successfully in the treatment of COPD, bronchiectasis, end-stage cancers, acute respiratory failure in COVID-19 infection and patients who cannot be intubated.

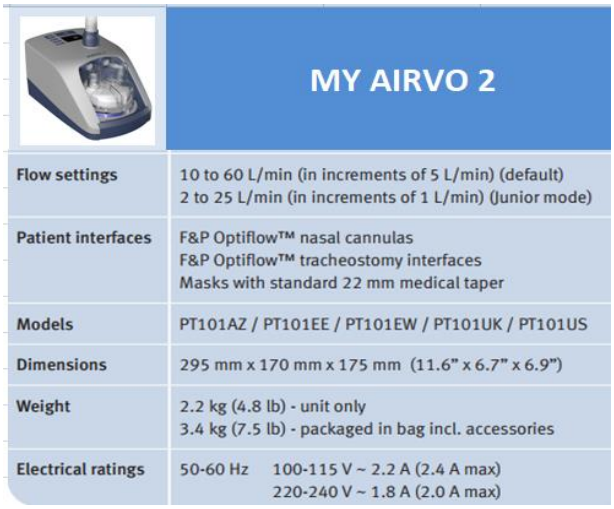
Use of the C-Flow mode

The C-FLow mode is suitable for use in hospitals, medical centres or at home.

Similarity of the clinical application of the device is demonstrated with the following devices:

- myARIVO™ 2 (Fisher & Paykel Healthcare) ;
- Precision Flow Plus (Vapotherm).

*Figure 44: **EO-150 Ventilator** similar devices for the C-Flow ventilation mode*



MY AIRVO 2	
Flow settings	10 to 60 L/min (in increments of 5 L/min) (default) 2 to 25 L/min (in increments of 1 L/min) (Junior mode)
Patient interfaces	F&P Optiflow™ nasal cannulas F&P Optiflow™ tracheostomy interfaces Masks with standard 22 mm medical taper
Models	PT101AZ / PT101EE / PT101EW / PT101UK / PT101US
Dimensions	295 mm x 170 mm x 175 mm (11.6" x 6.7" x 6.9")
Weight	2.2 kg (4.8 lb) - unit only 3.4 kg (7.5 lb) - packaged in bag incl. accessories
Electrical ratings	50-60 Hz 100-115 V ~ 2.2 A (2.4 A max) 220-240 V ~ 1.8 A (2.0 A max)

Precision Flow Plus VAPOTHERM	
Flow settings	1 - 40 L/min
Patient interfaces	Pediatric/Adult Small MP1500 2.7- 40 L/mn
Patient interfaces	Adult (base) MA1700 4.8 - 40 L/mn
Dimensions	300 mm x 200 mm x 180 mm
Weight	4,81 Kg
Electrical rating	56-60Hz 100-115V _ 200 VA

3.10.4.2.4.1 Definition

As NIPPV is now standard care for many disorders, it is better understood and more easily managed. Hence, HMV is progressively making its way out of hospitals and into more comfortable settings for patients. This change remains relatively new and appropriate studies still need to be carried out to verify patients are not being put at risk and that this does not represent a heavier burden for the healthcare system (van den Biggelaar et al. 2020; E. I. Schwarz et Bloch 2019; Stieglitz et al. 2017).

HMV has been widely developed since the beginning of the 21st century to increase patient comfort but also to help free up overcrowded healthcare establishments. As mentioned previously, PPV is now well understood and standard practice for many disorders. HMV can be used by many types of patients with varying ventilation needs, from nocturnal use only for sleep disorders to continuous use for patients with severely impaired breathing capacities such as late stage COPD or NMDs. Thus, ventilation itself is well accepted for the treatment of the indications mentioned above, but it is the home context of HMV that could cause issue if improperly used (E. I. Schwarz et Bloch 2019). Portable mechanical ventilators are generally more compact and lightweight devices that are easier to use and device parameters are set up with the help of a healthcare professional.

New questions have arisen from applying artificial ventilation at home, new evaluation criteria have been set up and new methods of care are being put in place to continuously improve HMV (Ergan et al. 2019). It seems telemedicine or tele-assistance are indeed effective in preventing hospitalisations but it does require the set-up of adequate resources, management tools (eg myCOPD), monitoring devices (Rabec et al. 2016; Vitacca et al. 2009) and 24h on-call healthcare professionals available to help patients with often life-threatening ailments (NICE, myCOPD management guideline 2022; Vitacca et al. 2009).

3.10.4.2.4.2 Indications and Posology

Indications for HMV are identical to those prescribed for classical in-hospital MV i.e. respiratory insufficiency. HMV is intended to treat chronic hypercapnia found in the following diseases:

- COPD (Ergan et al. 2019; Majorski et al. 2021; Raveling et al. 2021; Ribeiro et al. 2021; E. I. Schwarz et Bloch 2019; Suh, Murphy, et Hart 2019b) ;
- OHS (Ribeiro et al. 2021; E. I. Schwarz et Bloch 2019; Simonds 2016) ;
- NMDs (HAS, invasive ventilation in NMDs 2020; HAS, recommendations for HMV in NMDs 2006; E. I. Schwarz et Bloch 2019; Simonds 2016; Wolfram Windisch et al. 2018) ;
- CWDs (van den Biggelaar et al. 2020; E. I. Schwarz et Bloch 2019; Wolfram Windisch et al. 2018).

It should be noted that the *c-flow* ventilation mode, a type of HFNC therapy, is meant for all the above mentioned indications but especially for patients during acute respiratory exacerbations of COPD (Alnajada et al. 2021; Huang et al. 2021; L. Pisani et al. 2019; Yang, Yu, et Chen 2021) and COVID-19 infection (Agarwal et al. 2020; Boutron et al. 2020; Y. He et al. 2022; NICE - COVID-19 management guideline 2022; Ogawa et al. 2021; D.-Y. Xu et al. 2022).

The posology used for HMV is the same as the one prescribed for in-hospital MV.

Table 28: Posology used of HMV

Reference	Indication	Device studied	Ventilation type	Ventilation mode	Posology/ventilator settings	Time of use
(Markstro¨m et al. 2002) Retrospective study	Postpolio dysfunction, NMD, scoliosis and other	HMV	NIV (66%) and IV (34%)	PPV	ns	ns
(Wolfram Windisch et al. 2003) Protocol validation study	COPD, kyphoscoliosis, post-tuberculosis sequelae, OHS, poliomyelitis sequelae, phrenic nerve lesion, central hypoventilation syndrome, and patients with NMDs (DMD, polyneuropathy, myopathy, and ALS)	Pressure limited- or volume limited- HMV	NIV	PPV	ns	9.0±3.4 hours per day
(Chu et al. 2004) Multi-centre retrospective study.	COPD with chronic hypercapnic respiratory failure (CHRF); RTD; complicated OSA	HMV, bi-level pressure-support ventilators	NIV (94.8%) or invasive (5.2%)	Bi-level pressure-support ventilation	ns	ns
(Schönhofer et al. 2006)	COPD patients with CHRF	HMV BiPAP-ST; Respironics; Murrysville, PA	NIV	Pressure-cycled in controlled mode (BiPAP)	Inspiratory positive airway pressure of 19.0 ± 2.5 cm H_2O	Median 7.21 hours per night
(Vitacca et al. 2006) Pilot study	Chronic respiratory failure (CRF): COPD, RTD), NMD, ALS and other	HMV	NIV (65%) or invasive (35%)	ns	- Oxygen at discharge: 1.3 L/min (±1) - Maximum inspiratory pressure: 36 ±15 cmH_2O - Maximum expiratory pressure: 38 ±19 cmH_2O	ns
(Doménech-Clar et al. 2008)	Restrictive ventilatory disorders: NMD or thoracic	HMV	NIV	ns	ns	2 hours in the morning, 2 hours in

Reference	Indication	Device studied	Ventilation type	Ventilation mode	Posology/ventilator settings	Time of use
Prospective study	cage disorders, OHS or diaphragmatic relaxation					the afternoon and night ventilation
(López-Campos et al. 2008) Observational cross-section study	OHS, thoracic cage abnormalities, NMD, COPD and sequelae of tuberculosis	HMV	NIV	Pressure- (80.7%) or volume-ventilation (19.3%)	- LTOT: mean flow 1.5±0.5L/min - LTOT and supplemental oxygen: mean flow 1.6±0.6L/min	Mean 8.6 hours per day (±3.2)
(W. Windisch 2008)	COPD, RTD, NMD, OHS and other	HMV	NIV	Pressure-limited ventilation (76.5%) and volume-limited ventilation (23.5%)	- IPAP (cm H_2O): 25±6 (COPD), 20±4 (RTD), 19±4 (NMD) and 23±3 (OHS) - EPAP (cm H_2O): 1±2 (COPD), 3±2 (RTD), 1±2 (NMD) and 1±2 (OHS)	6.5 ± 2.1 hours per day
(Dogan et al. 2010)	CRF patients (mostly COPD)	HMV with BiPAP ventilation mode	NIV	BiPAP ventilation mode	- Mean IPAP (cm H_2O): 10.3±1.7 - Mean EPAP (cm H_2O): 4.2±0.4	Mean 4.0±2.6 hours per day
(Racca et al. 2011) Observational multi-centre study	NMD, lung and upper respiratory tract disease, hypoxic (ischemic) encephalopathy, abnormal ventilation control, spinal cord injury, chest anomalies and other	HMV	NIV (85%) and IV (15%)	PPV	- At 6 weeks 3h41min±1h41min - At 3 months 4h30min±1h44min ns	- ≤12 hours per day (57%) - ≥12 hours per day (43%)
(Storre et al. 2014)	COPD or CHRF	HMV Vivo 40 or Vivo 50 ventilator (Breas Medical, Mo¨lnlycke, Sweden)	NIV	HI-NIV or target tidal volume NIV (target V_T NIV)	- HI-NIV: 1.9±1.1 L/min; IPAP 25.7±6.2 cm H_2O and EPAP 5.1±1.7 cm H_2O - target V_T NIV: 1.9±1.1 L/min; minimal IPAP 20.7±6.2cm H_20; maximal IPAP 35.3±0.9 cm	At least 6 hours per night

Reference	Indication	Device studied	Ventilation type	Ventilation mode	Posology/ventilator settings	Time of use
					H_2O and EPAP 5.1±1.7 cm H_2O	
(Huttmann, Windisch, et Storre 2015)	severe CRF: NMD, COPD, overlapping COPD and OHS and destroyed lungs and other	HMV	IV	ns	- LTOT: 1.9±1.0 (NMD) and 2.7±1.2 (Lung disease) - IPAP:17.5±5 cm H_2O (NMD) and 25±8 cm H_2O (Lung disease) - EPAP: 5±2 cm H_2O (NMD) and 6±2 cm H_2O (Lung disease)	20 hours per day (NMD) and 18 hours per day (Lung disease)
(MacIntyre et al. 2016) SR 1 RCT and 25 observational studies	NMD, RTD, OHS and other	HMV	NIV (85%) and IV (15%)	ns	ns	ns
(P. B. Murphy et al. 2011; 2016; P. B. Murphy, Arbane, Phillips, et al. 2017; P. B. Murphy, Arbane, Bisquera, et al. 2017) Randomised controlled trial *UK HOT-HMV trial*	COPD with AHRF following exacerbation	HMV	HOT vs HMV	ns	- Discharge IPAP (cm H_2O): 26±3 (HMV group) - Discharge EPAP (cm H_2O): 5±1 (HMV group)	- At 6 weeks 3h41min±1h41min - At 3 months 4h30min±1h44min
(Povitz et al. 2018) Retrospective cohort study	RTD (kyphoscoliosis, fibrothorax, thoracoplasty, obesity, thoracic resection) and NMDs (ALS, muscular dystrophy, diaphragmatic	HMV	NIV (92.3%) and IV via tracheostomy (7.7%)	ns	ns	ns

Reference	Indication	Device studied	Ventilation type	Ventilation mode	Posology/ventilator settings	Time of use
	paralysis, myasthenia gravis, Guillain–Barre´ syndrome, spinal cord injury, stroke/transient ischemic attack, multiple sclerosis (MS), Parkinson's disease, neuropathy, post-polio syndrome, spina bifida, spinal muscular atrophy and other), COPD without other indication, unknown indication					
(Tan et al. 2018) A retrospective, single-centre cohort study	NMD, Pulmonary disease (PULM), non-NMD neuromuscular and chest wall disorders (NMCW) and OHS	HMV	NIV (99.2%) and IV via tracheostomy (0.8%)	Bi-level pressure-cycled PPV	- IPAP (cm H_2O): 14±2 (NMD), 18±3 (PULM), 17±3 (NMCW) and 20±3 (OHS) - EPAP (cm H_2O): 6±2 (NMD), 9±3 (PULM), 9±3 (NMCW) and 12±3 (OHS)	Use more than 4 hours per day: 70% (NMD), 88% (PULM), 84% (NMCW) and 78% (OHS)
(E. I. Schwarz et al. 2020)	NMD or CWD, COPD, OHS, overlap of COPD and OSA and other	HMV	NIV (88%) and IV via tracheostomy (12%)	Pressure support ventilation (PSV, 62%) or pressure controlled (PCV, 34%)	- Mean IPAP: 21.9±7.6 cm H_2O - Mean EPAP: 6.6±5.7 cm H_2O	Average use 9.6±7.7 hours per day
(Valko et al. 2020) Single-centre prospective observational study	COPD, restrictive CWD, OHS, non-progressive NMD, progressive NMD	A40 or Trilogy 100 HMV (Philips)	NIV (78.8%) and VI via tracheostomy (21.2%)	NIV, O_2 therapy, CPAP, Bi-level PAP, AVAPS, HI-NIV or LTOT	- Oxygen flow: 1.8±2.8 L/min - Mean IPAP: 22.29±4.8 cm H_2O - Mean EPAP: 8.3±3.6 cm H_2O	12.6 ±6.5 hours per day

Reference	Indication	Device studied	Ventilation type	Ventilation mode	Posology/ventilator settings	Time of use
(van den Biggelaar et al. 2020) Randomised trial	ALS, Diaphragm paralysis, Myotonic Dystrophy (MD), Progressive Spinal Muscular atrophy (PSMA), OHS, Restriction/scoliosis, Facioscapulohumeral dystrophy (FSHD), Hereditary Motor and Sensory Neuropathy (HMSN), Multiple Synostosis Syndrome, MS, Becker muscular dystrophy, Spinal Muscular Atrophy (SMA), post-polio syndrome and myofibrillar myopathies	ResMed ASTRAL 100/150 or ResMed Elisée	NIV	Spontaneous/Timed ventilation mode	- IPAP (cm H_2O): 16.8±4.6 (hospital group) vs 16.0±3.7(home group) - EPAP (cm H_2O): 5.8±1.8 (hospital group) vs 5.4±1.7(home group)	6.6 ±3.0 hours per night
(Wilson et al. 2020) SR and MA 33 studies	CHRF due to COPD	HMV or BPAP device	Noninvasive ventilation (NIV)	BPAP spontaneous/timed, spontaneous, volume-assured pressure support ventilation (VAPSV), PCV or not specified	ns	Not specified (≥ 4 hours per day)
(Maquilón et al. 2021) Prospective study	CRF, COPD, OHS, NMD, non-cystic fibrosis bronchiectasis or tuberculosis (non-CF BC or TBC), scoliosis and ALS.	HMV	NIV (94.8%) and VI via tracheostomy (5.2%)	- spontaneous/timed: 86.8% - spontaneous (S): 4.8% - Hybrid (AVAPS or IVAPS): 6.5% - other modes (controlled assist mode, synchronous	- Median IPAP: 16 (14-18) cm H_2O - Median EPAP: 6 (6-8) cm H_2O - Median maximal IPAP (only for hybrid mode): 18 (16-22) cm H_2O	Average 7.3 hours (5.8-8.8) per day

Reference	Indication	Device studied	Ventilation type	Ventilation mode	Posology/ventilator settings	Time of use
				intermittent mandatory ventilation, pressure control and volume control): 1.8%		

In summary, most of the studies involve noninvasive ventilation on patients with a wide range of illnesses, the most common are: COPD, NMD and OHS. Other indications are less common but still noteworthy such as post-polio and tuberculosis sequalae, chest wall abnormalities and RTDs. Pressure-control ventilations modes (notably BiPAP) were the most included in the studies, although data involving new hybrid ventilation modes (AVAPS or VAPSC) was also reported. The average use of the HMV is around 9 hours per day but this is highly dependent on the indication. Overall posology measures including IPAP (mean 20 cm H_2O), EPAP (mean 5.4 cm H_2O) and oxygen flow (mean 1.7 L/min) also depend on the indication.

Table 29: Posology of high-flow oxygen therapy

Reference	Indication	Device studied	Ventilation type	Ventilation mode	Posology	Time of use
(Okuda et al. 2014) Case report	COPD exacerbations	Nasal high-flow oxygen therapy system: MH-2000 heated humidifier (Pacific-Medico) and a Vivo 30 ventilator (Breas Medical AB),	Noninvasive via nasal cannula	HFNC therapy+BiPAP ventilation modes then HFNC+CPAP	- HFNC oxygen airflow: ≥30 L/min - IPAP (cm H_2O): 10.0 - EPAP (cm H_2O): 4.0	ns
(Lara Pisani et al. 2017) Randomised physiologic study	COPD and CHRF	NIV and HHNC (Airvo 2; Fisher & Paykel Healthcare, Auckland, New Zealand)	Noninvasive via nasal cannula	HFNC vs NIV	HFNC: 20 L/min (37°C)	30 min+10min standard oxygen therapy
(Vogelsinger et al. 2017) Prospective study	COPD with stable hypoxemia	Nasal high-flow oxygen therapy system: TNI®20 oxy (TNI medical AG, Würzburg, Germany)	Noninvasive via nasal cannula	HFNC vs COT	- Conventional Oxygen Therapy (COT): titrated oxygen airflow from 0.5L/min until PaO_2 was ≥60 mmHg or PaO_2 ≥10 mmHg - HFNC therapy: titrated oxygen airflow from 15L/min	60 mins per therapy

Reference	Indication	Device studied	Ventilation type	Ventilation mode	Posology	Time of use
					until PaO_2 was ≥60 mmHg or PaO_2 ≥10 mmHg (37°C)	
(Longhini et al. 2019) Randomised crossover physiologic study	COPD with hypercapnic acute respiratory failure treated with NIV	Ventilator Servo-I (Maquet Critical Care, Solna, Sweden) and heated humidifier (Optiflow and MR850; Fisher & Paykel Healthcare, Auckland, NZ	Noninvasive via nasal cannula	HFNC vs COT	- HFNC oxygen flow rate: 50 L/min (37°C) - COT: IPA 10.5±21 cm H_2O and EPAP 5.4±1.6 cm H_2O	30-min HFNC therapy sessions
(Rezaei et al. 2021) Randomised clinical trial	Acute Exacerbation of COPD (AECOPD)	Nasal high-flow oxygen therapy system: TNI medical AG (Würzburg)	Noninvasive via nasal cannula	HFNC vs NIV (VPAP)	- HFNC oxygen airflow 15-35 L/min (37°C)	30-min HFNC or NIV therapy sessions
(Z. Xu et al. 2021a) MA and SR (25 studies)	COVID-19	ns	Noninvasive via nasal cannula	HFNC vs NIV	ns	ns

High-flow oxygen therapy ventilation mode is used to treat acute respiratory failure mostly in the case of COVID-19 or exacerbation phases of COPD. All the studies included involved NIV. HFOT is usually 30-min therapy sessions (sometime 60 mins) or it can also be following by a short session of convention ventilation therapy (10 mins). Typical oxygen airflow was between 20 and 50 L/min (37°C).

3.10.4.3 Users

The users are the patients themselves (children and adults), but for children the users are the parents or legal guardians. During the adaptation stage or other significant setting changes, such as weaning, the ventilator is handled by a healthcare provider.

3.10.4.4 Patient typology

In the same way as with MV performed in the hospital, HMV is recommended for patients with respiratory failure of all ages, including very young neonatal babies (Comer, Oakes, et Mukherjee 2015; P. Murphy et Hart 2009; NICE, Neonatal respiratory support guideline 2019). The following table summarises the patient typology for HMV identified in the studies used in this section.

Table 30: Typology of patients using HMV

Reference	Indication	Number	Age	Gender (M/F)	Follow-up
(Markstro¨m et al. 2002) Retrospective study	Postpolio dysfunction, NMD, scoliosis and other	91 patients: postpolio dysfunction (n=33), NMD (n=16), scoliosis (n=13) and other	Adults (mean 58.8 ±1.6)	40/51	Once a year (NIV) or once a month (IV)
(Wolfram Windisch et al. 2003) Protocol validation study	COPD, kyphoscoliosis, post-tuberculosis sequelae, OHS, poliomyelitis sequelae, phrenic nerve lesion, central hypoventilation syndrome and NMDs (DMD, polyneuropathy, myopathy, and ALS)	226 patients with CRF: COPD (n=78), kyphoscoliosis (n=57), post-tuberculosis sequelae (n=20), OHS (n=12), poliomyelitis sequelae (n=4), phrenic nerve lesion (n=3), central hypoventilation syndrome (n=3) and NMDs (n=49)	Adults (mean 57.3 ±14.0)	118/108	One routine follow up visit (not specified)
(Chu et al. 2004) Multi-centre retrospective study.	COPD with CHRF, RTD, complicated OSA	249 patients: COPD with CHRF (n=121), RTD (n=85), complicated OSA (n=43)	Adults (mean 62.7 ±13.8)	156/93	3 years
(Schönhofer et al. 2006)	COPD patients with CHRF	25 patients	Adults (mean 60.0 ±10.4)	14/11	2 months
(Vitacca et al. 2006) Pilot study	CRF: COPD, RTD, NMD, ALS and other	45 patients: COPD (n=17), RTD (n=6), NMD (n=13), ALS (n=5) other (n=4)	Adults (mean 59 ±19)	30/15	176 days (±69)
(Doménech-Clar et al. 2008) Prospective study	Restrictive ventilatory disorders: NMD or thoracic cage disorders, OHS or diaphragmatic relaxation	42 patients	Adults (mean 59 ±17.3)	16/26	3- and 6- months
(López-Campos et al. 2008) Observational cross-section study	OHS, thoracic cage abnormalities, NMD, COPD and sequelae of tuberculosis	115 patients: OHS (n=37), thoracic cage abnormalities (n=33), NMD (n=18), COPD (n=15) and sequelae of tuberculosis (n=12)	Adults (mean 61.9 ±13.9)	57/58	One year

Reference	Indication	Number	Age	Gender (M/F)	Follow-up
(W. Windisch 2008)	COPD, RTD, NMD, OHS and other	85 patients: COPD (n=27), RTD (n=29) and NMD (n=17), OHS (n=9) and others (n=3)	Adults (mean 59.0 ±11.25)	52/33	1- and 12- months
(Dogan et al. 2010)	CRF patients (mostly COPD)	170 patients in total, 56 patients still alive for last follow up	Adults (mean 62.05 ±10.46)	35/21	1 to 5 years
(Racca et al. 2011) Observational multi-centre study	NMD, lung and upper respiratory tract disease, hypoxic (ischemic) encephalopathy, abnormal ventilation control, spinal cord injury, chest anomalies and other	362 patients: NMD (n=178), chronic lung and upper respiratory tract disease (n=64), hypoxic (ischemic) encephalopathy (n=48) and abnormal ventilation control (n=44), spinal cord injury (n=11), chest anomalies (n=16) and other (n=1)	Children up to 17 years old (median age 8; interquartile range 4-14)	203/159	Trend over time (ns)
(Storre et al. 2014)	COPD or chronic hypercapnic respiratory failure	10 patients	Adults (mean 64.5 ±8.5)	5/5	One routine follow up visit (not specified)
(Huttmann, Windisch, et Storre 2015)	Severe CRF: NMD, COPD, overlapping COPD and OHS and destroyed lungs and other	32 patients: NMD (n=14), COPD (n=11), overlapping COPD and OHS (n=2) and destroyed lungs (n=1), other non-classified (n=4)	Adults (mean 59.1 ±14)	15/17	One follow up (up to 6 months)
(MacIntyre et al. 2016) SR 1 RCT and 25 observational studies	NMD, RTD, OHS and other	4425 patients with CRF: (NMD) (n=1697), RTD (n=481), OHS (n=293), other (n=748) and not specified (n=1211)	Adults (mean 60)	1880/2545	ns
(P. B. Murphy et al. 2011, 2016; 2016; P. B. Murphy, Arbane, Phillips, et al. 2017; P. B. Murphy, Arbane, Bisquera, et al. 2017) Trial UK HOT-HMV	COPD with AHRF following exacerbation	116 COPD patients: (n=59) HOT group and (n=57) HMV group	Adults (median 67±10)	ns	Up to a year follow up

Reference	Indication	Number	Age	Gender (M/F)	Follow-up
(Povitz et al. 2018) Retrospective cohort study	RTDs (kyphoscoliosis, fibrothorax, thoracoplasty, obesity, thoracic resection), NMDs (ALS, muscular dystrophy, diaphragmatic paralysis, myasthenia gravis, Guillain–Barre´ syndrome, spinal cord injury, stroke/transient ischemic attack, MS, Parkinson's disease, neuropathy, post-polio syndrome, spina bifida, spinal muscular atrophy and other), COPD without other indication, unknown indication	4670 patients: RTD (kyphoscoliosis (n=51), fibrothorax (n=117), thoracoplasty (n=9), obesity (n=743), thoracic resection (n=14)) and NMDs (ALS (n=350), muscular dystrophy (n=317), diaphragmatic paralysis (n=37), myasthenia gravis (n=294), Guillain–Barre´ syndrome (n=9), spinal cord injury (n=247), stroke/transient ischemic attack (n=51), MS (n=131), Parkinson's disease (n=47), neuropathy (n=37), post-polio syndrome (n=9), spina bifida (n=23), spinal muscular atrophy (n=9) and other (n=19)), COPD without other indication (n=878), unknown indication (n=1690)	Adults (mean 58.5 ±14.6)	2788/1882	Trend over time (12 years)
(Tan et al. 2018) A retrospective, single-centre cohort study	NMD, Pulmonary disease, non-NMD neuromuscular and chest wall disorders (NMCW) and OHS	240 patients: NMD (n=93), pulmonary disease (n=60), non-NMD neuromuscular and NMCW (n=51) and OHS (n=36)	Adults (mean 58.28)	145/95	Trend over time (5 years)
(E. I. Schwarz et al. 2020)	NMD or CWD, COPD, OHS, overlap of COPD and OSA and other	1210 CHRF patients: NMD or CWD (both groups n=533), COPD (n=296), OHS (n=202), overlap of COPD and OSA (n=52) and other (n=127)	Adults (mean 65.1 ±15.2)	671/539	Trend over time (10 years)
(Valko et al. 2020) Single centre prospective observational study	COPD, restrictive chest wall disease, OHS, non-progressive NMD, progressive NMD	66 CRF patients: COPD (n=9), restrictive chest wall disease (n=5), OHS (n=20), non-progressive NMD (n=19), progressive NMD (n=13)	Adults (mean 51.5 ±18.1)	46/20	6 months
(van den Biggelaar et al. 2020) Randomised trial	ALS, Diaphragm paralysis, Myotonic Dystrophy (MD), PSMA, OHS, Restriction/scoliosis, FSHD, Hereditary Motor and Sensory Neuropathy (HMSN),	95 CHR insufficiency patients: ALS (n=42), Diaphragm paralysis (n=15), MD (n=12), PSMA (n=5), OHS (n=5), Restriction/scoliosis (n=6), FSHD (n=2), HMSN (n=1), Multiple Synostosis	Adults (mean 56.9 ±12.9)	66/29	6 months

Reference	Indication	Number	Age	Gender (M/F)	Follow-up
	Multiple Synostosis Syndrome, MS, Becker muscular dystrophy, SMA, post-polio syndrome and myofibrillar myopathies	Syndrome (n=1), MS (n=2), Becker muscular dystrophy (n=1), SMA (n=1), post-polio syndrome (n=1) and myofibrillar myopathies (n=1)			
(Wilson et al. 2020) SR and MA 33 studies	CHRF due to COPD	51085 patients	Adults (mean 65.7 ±2.1)	29119/21966	Various follow up timepoints (up to 3 years)
(Maquilón et al. 2021) Prospective study	CRF, COPD, OHS, NMD, non-cystic fibrosis bronchiectasis or tuberculosis (non-CF BC or TBC), scoliosis and ALS	1105 CRF patients: COPD (n=388), OHS (n=264), NMD (n=180), non-cystic fibrosis bronchiectasis or tuberculosis (non-CF BC or TBC, n=92), scoliosis (n=65) and ALS (n=58) and other (n=58)	Adults (median 59 ±24)	463/642	Trend over time (up to 9 years)

The most common indications for conventional ventilation modes of HMV are COPD, NMDs, OHS and CWDs. Overall age of patients using HMV is usually late 50s to 60s. Nevertheless, it is highly dependent on age as NMD and CWD patients are usually diagnosed younger than COPD or OHS.

Table 31: Typology of patients using high flow oxygen therapy

Reference	Indication	Number	Age	Gender (M/F)	Follow-up
(Okuda et al. 2014) Case report	COPD exacerbations	1 patient	Adult (73)	0/1	Trend over time (ns)
(Lara Pisani et al. 2017) Randomised physiologic study	COPD and CHRF	14 patients	Not specified	Not specified	Five separate treatment trials – no follow up
(Vogelsinger et al. 2017) Prospective study	CODP with stable hypoxemia	77 patients: normocapnic COPD (n=50) and hypercapnic COPD (n=27)	Adults (mean 66.2 ±8.5)	57/20	1 hour after treatment
(Longhini et al. 2019)	COPD with hypercapnic acute respiratory failure treated with NIV	30 patients	Adults (mean 72.5 ±8.2)	17/13	Five separate treatment trials – no follow up

Reference	Indication	Number	Age	Gender (M/F)	Follow-up
Randomised crossover physiologic study					
(Rezaei et al. 2021) Randomised clinical trial	AECOPD	30 patients	Adults (mean 61.3 ±9.3)	24/6	3 months
(Z. Xu et al. 2021a) MA and SR (25 studies)	COVID-19	2851 patients	Adults	Not specified	Not specified

The most common indications for high-flow oxygen therapy are COPD (chronic and during cute exacerbation phases) and acute COVID-19 respiratory failure.
Overall age of patients undergoing high flow oxygen therapy is late 60s to 70s.

3.10.4.5 HMV evaluation criteria

Regardless of the indication for which HMV is used, the same major categories of tests : physiological measures (criteria relative to breathing function, gas dosages etc.) as well as QoL criteria (sleep, HRQL tests, physical capabilities etc.). Assessment tools are improving in order to better evaluate performance and safety of HMV compared to in-hospital MV or no ventilation.

Table 32: Summary of HMV evaluation criteria

Physiological measures		
Evaluation criteria		**Reference**
Arterial blood gas (ABG)	Bicarbonate (HCO_3)	(Altintas 2016; Arellano-Maric et al. 2020; Callegari et al. 2017; Coleman, Wolfe, et Kalhan 2019; Doménech-Clar et al. 2008; Duiverman et al. 2020; 2020; Kaw et al. 2009; Kopsaftis et al. 2020; de Lucas-Ramos et al. 2004; Mokhlesi et al. 2019; P. B. Murphy et al. 2011; Palm et al. 2016; Ramsay et al. 2015; Raveling et al. 2018; 2020; Ribeiro et al. 2021; Schönhofer et al. 2006; S. B. Schwarz et al. 2018a; F. M. Struik et al. 2014; Suh, Murphy, et Hart 2019a; W. Windisch 2008; Wolfram Windisch et al. 2018)
	Daytime and/or night-time $PaCO_2$	(Alnajada et al. 2021; van den Biggelaar et al. 2020; COPD Working Group 2012; Duiverman et al. 2020; Elshof et Duiverman 2020; Ergan et al. 2019; Huang et al. 2021; Kopsaftis et al. 2020; Lewis et al. 2021; Longhini et al. 2019; de Lucas-Ramos et al. 2004; P. B. Murphy et al. 2011; Ogawa et al. 2021; Okuda et al. 2014; Pallero et al. 2014; Palm et al. 2016; Lara Pisani et al. 2017; L. Pisani et al. 2019; Raveling et al. 2021; Rezaei et al. 2021; Ribeiro et al. 2021; E. I. Schwarz et Bloch 2019; S. B. Schwarz et al. 2018a; F. M. Struik et al. 2014; Vogelsinger et al. 2017; Wijkstra et al. 2002; D.-Y. Xu et al. 2022; Z. Xu et al. 2021b; Yang, Yu, et Chen 2021)
	Daytime and/or night-time PaO_2	(Alnajada et al. 2021; COPD Working Group 2012; Elshof et Duiverman 2020; Ergan et al. 2019; Y. He et al. 2022; Huang et al. 2021; Longhini et al. 2019; de Lucas-Ramos et al. 2004; P. B. Murphy et al. 2011; Ogawa et al. 2021; Okuda et al. 2014; Pallero et al. 2014; Palm et al. 2016; L. Pisani et al. 2019; Raveling et al. 2021; Ribeiro et al. 2021; E. I. Schwarz et Bloch 2019; S. B. Schwarz et al. 2018a; F. M. Struik et al. 2014; 2014; Vogelsinger et al. 2017; Wijkstra et al. 2002; D.-Y. Xu et al. 2022; Z. Xu et al. 2021b; Yang, Yu, et Chen 2021; Zhang et al. 2020a)
	Oxygen saturation levels (SaO_2)	(Lewis et al. 2021; Pallero et al. 2014; Rezaei et al. 2021; Zhang et al. 2020a)
	pH	(Alnajada et al. 2021; Elshof et Duiverman 2020; Longhini et al. 2019; Okuda et al. 2014; Pallero et al. 2014; S. B. Schwarz et al. 2018a; F. M. Struik et al. 2014; Yang, Yu, et Chen 2021; Zhang et al. 2020a)
Blood D-dimer (COVID-19)		(Z. Xu et al. 2021b)
Blood lactate concentration (COVID-19)		(Z. Xu et al. 2021b)
Body Mass Index (BMI)		(Hitzl et al. 2010; P. B. Murphy et al. 2011; Ribeiro et al. 2021; D.-Y. Xu et al. 2022)
Costs		(van den Biggelaar et al. 2020; Elshof et Duiverman 2020; Pallero et al. 2014)

Day of first exacerbation	(Elshof et Duiverman 2020)
Diaphragm displacement (DD)	(Longhini et al. 2019)
Diaphragm mobility during quiet breathing	(Yang, Yu, et Chen 2021)
Diaphragm Thickening Fraction (TF)	(Elshof et Duiverman 2020; Longhini et al. 2019; Yang, Yu, et Chen 2021)
Diaphragm thickness at end-inspiration ($Thick_{insp}$)	(Longhini et al. 2019)
Diaphragm thickness diaphragm thickness at end-expiration ($Thick_{exp}$)	(Longhini et al. 2019)
Diaphragmatic-rapid shallow breathing index	(Yang, Yu, et Chen 2021)
Droplet dispersion (COVID-19)	(Agarwal et al. 2020; Ogawa et al. 2021)
Dyspnoea	(Alnajada et al. 2021; COPD Working Group 2012; Duiverman et al. 2020; Elshof et Duiverman 2020; Ergan et al. 2019; Kopsaftis et al. 2020; Lewis et al. 2021; P. B. Murphy et al. 2011; 2016; P. B. Murphy, Arbane, Phillips, et al. 2017; P. B. Murphy, Arbane, Bisquera, et al. 2017; Raveling et al. 2021; Rezaei et al. 2021; 2021; Ribeiro et al. 2021; Stieglitz et al. 2017; F. M. Struik et al. 2014; Wilson et al. 2020)
End-inspiration diaphragm thickness	(Yang, Yu, et Chen 2021)
Expiratory/Inspiratory time (Te) and (Ti)	(Lara Pisani et al. 2017)
Forced expiratory volume in 1s (FEV_1)	(COPD Working Group 2012; Duiverman et al. 2020; Elshof et Duiverman 2020; Ergan et al. 2019; Kopsaftis et al. 2020; de Lucas-Ramos et al. 2004; P. B. Murphy et al. 2011; Pallero et al. 2014; Raveling et al. 2021; F. M. Struik et al. 2014; Wijkstra et al. 2002)
Forced vital capacity (FVC)	(Duiverman et al. 2020; Kopsaftis et al. 2020; de Lucas-Ramos et al. 2004; P. B. Murphy et al. 2011; Pallero et al. 2014; Raveling et al. 2021; Wijkstra et al. 2002)
Fraction of inspired oxygen (FiO_2)	(Y. He et al. 2022; Ogawa et al. 2021; Lara Pisani et al. 2017)
Initiation of HMV setting (hospital vs domiciliary)	(Ribeiro et al. 2021)
Inspiration effort	(Rezaei et al. 2021)
Lung function	(Duiverman et al. 2020; Ergan et al. 2019; Kopsaftis et al. 2020; P. B. Murphy et al. 2011; 2016; P. B. Murphy, Arbane, Phillips, et al. 2017; P. B. Murphy, Arbane, Bisquera, et al. 2017; Pallero et al. 2014; Raveling et al. 2021; Ribeiro et al. 2021; F. M. Struik et al. 2014; Wijkstra et al. 2002)
Maximal expiratory pressure (PEmax)	(Pallero et al. 2014; Raveling et al. 2021)
Maximal inspiratory pressure (PImax)	(Pallero et al. 2014; Raveling et al. 2021; Wijkstra et al. 2002)
Minute Volume (V_E)	(de Lucas-Ramos et al. 2004; Zhang et al. 2020a)
Mortality / survival	(Agarwal et al. 2020; Alnajada et al. 2021; COPD Working Group 2012; Dretzke et al. 2016; Elshof et Duiverman 2020; Ergan et al. 2019; Y. He et al. 2022; Lewis et al. 2021; P. B. Murphy et al. 2011; 2016; P. B. Murphy, Arbane, Phillips, et al. 2017; P. B. Murphy, Arbane, Bisquera, et al. 2017; Ogawa et al. 2021; Raveling et al. 2021; Rezaei et al. 2021; Soghier et al. 2019; Stieglitz et al. 2017; F. M. Struik et al. 2014; Wilson et al. 2020; D.-Y. Xu et al. 2022; Z. Xu et al. 2021b; Yang, Yu, et Chen 2021)
Number /frequency of exacerbations (in COPD)	(Duiverman et al. 2020; Elshof et Duiverman 2020; Ergan et al. 2019; P. B. Murphy et al. 2011; 2016; P. B. Murphy, Arbane, Phillips, et al. 2017; P. B. Murphy, Arbane, Bisquera, et al. 2017; Raveling et al. 2021; Ribeiro et al. 2021; F. M. Struik et al. 2014; 2014; Wilson et al. 2020)

Peripheral oxygen saturation (SpO_2)		(Elshof et Duiverman 2020; Lewis et al. 2021; Okuda et al. 2014; Vogelsinger et al. 2017)
Rapid shallow breathing index		(Elshof et Duiverman 2020)
Ratio of inspiratory Time and total breathing cycle length (T_I/T_{TOT})		(de Lucas-Ramos et al. 2004)
Residual Volume		(Duiverman et al. 2020; Pallero et al. 2014; Raveling et al. 2021; Vogelsinger et al. 2017)
Respiratory rate (RR)		(Elshof et Duiverman 2020; Lewis et al. 2021; Longhini et al. 2019; L. Pisani et al. 2019; Rezaei et al. 2021; D.-Y. Xu et al. 2022; Yang, Yu, et Chen 2021)
Risk of intubation		(Yang, Yu, et Chen 2021)
ROX index (ratio SpO_2/FiO_2 to RR)		(Prakash et al. 2021; Z. Xu et al. 2021b; Zhou et al. 2022)
Residual volume/ Total Lung Capacity		(Pallero et al. 2014)
Tidal Volume (V_T)		(de Lucas-Ramos et al. 2004; Lara Pisani et al. 2017)
Total Lung Capacity (TLC)		(Duiverman et al. 2020; Pallero et al. 2014)
Tracheal intubation rate		(Agarwal et al. 2020; Alnajada et al. 2021; Y. He et al. 2022; Rezaei et al. 2021; D.-Y. Xu et al. 2022; Z. Xu et al. 2021b)
Transcutaneous Carbon Dioxide Tension ($PtcCO_2$)		(Aarrestad et al. 2016; Elshof et Duiverman 2020; Ergan et al. 2019; L. Pisani et al. 2019; E. I. Schwarz et Bloch 2019; S. B. Schwarz et al. 2018a; F. M. Struik et al. 2014; Zhang et al. 2020a)
Quality of Life		
Admission-free survival		(Raveling et al. 2021)
Anthopometrics		(P. B. Murphy et al. 2011; 2016; P. B. Murphy, Arbane, Phillips, et al. 2017; P. B. Murphy, Arbane, Bisquera, et al. 2017)
Effect on sleep	Pittsburgh Quality Sleep Questionnaire	(Arellano-Maric et al. 2020)
	Polysomnography (PSG)	(Okuda et al. 2014; Ribeiro et al. 2021; E. I. Schwarz et Bloch 2019; Zhang et al. 2020b)
	Sleep quality	(Ergan et al. 2019; Raveling et al. 2021; Wijkstra 2003; Wijkstra et al. 2002; Wilson et al. 2020; Zhang et al. 2020a)
	Sleep questionnaire	(P. B. Murphy et al. 2011, 2016; 2016, 2017; P. B. Murphy, Arbane, Phillips, et al. 2017; P. B. Murphy, Arbane, Bisquera, et al. 2017; Zhang et al. 2020a)
	Visual analogue scale (VAS)	(Zhang et al. 2020a)
Emergency department visits		(Pallero et al. 2014; Soghier et al. 2019; Wilson et al. 2020)
Emergency frequencies		(Stieglitz et al. 2017)
Epworth sleepiness Scale (ESS)		(Palm et al. 2016)
Health related quality of life	Acute Physiology and Chronic Health Evaluation (APACHE) score	(D.-Y. Xu et al. 2022)
	Assessment of Quality of Life questionnaire (AQoL-8D)	(Hannan et al. 2016)
	Chronic Respiratory Disease questionnaire	(Kopsaftis et al. 2020)
	Health Index (HI)	(Markstro¨m et al. 2002)
	Hospital Anxiety and Depression Scale (HADS)	(van den Biggelaar et al. 2020; Duiverman et al. 2020)
	Maugeri Respiratory Failure questionnaire (MRF26)	(Carone et al. 2016)

	Maugeri Respiratory Failure questionnaire-28 (MRF-28)	(Carone et al. 2016; Wijkstra et al. 2002)
	Medical Research Council scale (MRC)	(P. B. Murphy et al. 2011; 2016; P. B. Murphy, Arbane, Phillips, et al. 2017; P. B. Murphy, Arbane, Bisquera, et al. 2017)
	Sense of Coherence (SOC) Scale	(Markstro¨m et al. 2002)
	Sequential Organ Failure Assessment (SOFA)	(Y. He et al. 2022)
	Severe Respiratory Insufficiency (SRI) questionnaire	(Arellano-Maric et al. 2020; van den Biggelaar et al. 2020; Budweiser et al. 2007; Duiverman et al. 2020; Ergan et al. 2019; Hannan et al. 2016; Markstro¨m et al. 2002; P. B. Murphy et al. 2011; 2016; P. B. Murphy, Arbane, Phillips, et al. 2017; P. B. Murphy, Arbane, Bisquera, et al. 2017; Raveling et al. 2021; S. B. Schwarz et al. 2018a; F. M. Struik et al. 2014; 2014; Wolfram Windisch et al. 2003)
	Short Form Health Survey (SF-36)	(Carone et al. 2016; Duiverman et al. 2020; Ergan et al. 2019; Wijkstra et al. 2002; Zhang et al. 2020a)
	Sickness Impact Profile (SIP)	(Markstro¨m et al. 2002)
	St George's Respiratory Questionnaire (SGRQ)	(Carone et al. 2016; Ergan et al. 2019; Kopsaftis et al. 2020; P. B. Murphy et al. 2011; Raveling et al. 2021; Wijkstra et al. 2002; Zhang et al. 2020a)
	The Clinical COPD Questionnaire (CCQ)	(Duiverman et al. 2020)
ICU admissions		(Kopsaftis et al. 2020; Pallero et al. 2014; Wijkstra 2003; Wilson et al. 2020)
Incidence of nasal facial skin breakdown		(Z. Xu et al. 2021b)
Length of hospital stay		(Agarwal et al. 2020; COPD Working Group 2012; Elshof et Duiverman 2020; Y. He et al. 2022; Kopsaftis et al. 2020; Lewis et al. 2021; Ogawa et al. 2021; Pallero et al. 2014; Rezaei et al. 2021; S. B. Schwarz et al. 2018a; F. M. Struik et al. 2014; Z. Xu et al. 2021b)
Loudness		(Alnajada et al. 2021; L. Pisani et al. 2019)
Number of all-cause hospital admissions		(COPD Working Group 2012; Dretzke et al. 2016; Elshof et Duiverman 2020; Ergan et al. 2019; Kopsaftis et al. 2020; P. B. Murphy et al. 2011; 2016; P. B. Murphy, Arbane, Phillips, et al. 2017; P. B. Murphy, Arbane, Bisquera, et al. 2017; Pallero et al. 2014; Raveling et al. 2021; S. B. Schwarz et al. 2018a; F. M. Struik et al. 2014; Wilson et al. 2020)
Overall Comfort		(Alnajada et al. 2021; Longhini et al. 2019; Lara Pisani et al. 2017; L. Pisani et al. 2019; Yang, Yu, et Chen 2021)
Physical activity capacity	the endurance shuttle walk test (SWT)	(Zhang et al. 2020a)
	6-minute walk distance (6MWD) test	(COPD Working Group 2012; Duiverman et al. 2020; Ergan et al. 2019; Pallero et al. 2014; Raveling et al. 2021; Soghier et al. 2019; Wijkstra et al. 2002; Wilson et al. 2020)
	The constant work rate cycle test (CWRT)	(Elshof et Duiverman 2020)
	Patients autonomy (ability to perform all daily life activities) or modified Barthel index	(Ribeiro et al. 2021; Stieglitz et al. 2017; F. M. Struik et al. 2014)

Smoking status	(Pallero et al. 2014; Ribeiro et al. 2021; D.-Y. Xu et al. 2022)
Treatment duration	(Ogawa et al. 2021; D.-Y. Xu et al. 2022)
Weaning status	(Stieglitz et al. 2013)

The most commonly used physiological evaluation criteria for HMV were: ABGs measures, dyspnoea, breathing functions (*eg* RR and lung function). QoL was mostly assessed by HRQL questionnaires (*eg* SRI, SF-36 and SGRQ), physical activity capacity tests (*eg* 6MWD and patient autonomy test) and effects on sleep (*eg* PSG and sleep quality questionnaires).

3.10.4.6 HMV performance

In the treatment of COPD

Classical ventilation modes

An early meta-analysis (7 RCTs, n=245) by Wijkstra et al., assessed the effects of long-term HMV for COPD patients via nocturnal NIPPV (Wijkstra et al. 2002). After 3 months and 12 months of treatment, various measures including $PaCO_2$, 6MWD, HRQL, lung function, respiratory muscle strength and sleep efficiency were neither clinically nor statistically significant in this study. The authors claim the quality of the results are moderate and do not consider this type of therapy to be beneficial to COPD patients.

A safety and performance study of HMV for patients (n=17) treated with IV showed that although respiratory incidents are common in HMV, it was possible to safely treat patients with the adequate resources (Stieglitz et al. 2013). Most interventions were carried out by nursing staff and involved the use of a bag valve mask (n=16) or replacing the tracheal canula (n=7). The vast majority of patients had COPD (n=12) and the remaining had NMD (n=5) that led to invasive HMV.

A randomised, controlled, parallel-group study by Struik et al. on COPD patients having been prescribed long-term NIV (LT-NIV) after acute respiratory failure assessed NIV efficacy (F. M. Struik et al. 2014). A comparison of NIV treated-patients (n=101) versus patients treated with COT (n=100) found no significant difference when comparing hospital admission rates one year after discharge (65% vs 64%), long term survival (63 vs 58 deaths), annual median of exacerbations (range) (1.0 (0-9) vs 2.0 (0-14); p=0.26), mean FEV1, vital capacities, activities of daily living, anxiety/depression scores and dyspnoea. Nevertheless, survival was significantly longer for NIV group compared to conventional treatment (299 days vs 291 days; p=0.99), as well as the nocturnal $PtcCO_2$ after 12 months (mean difference −0.6 kPa (95% CI −1.1 to −0.1; p=0.03)) and SRI-assessed HRQL which showed a clear improvement of 'social relationships' and sleep (p=0.054). It must be noted that the data is on a small cohort and should be confirmed with additional data.

Dretzke et al. published a meta-analysis and systematic review (31 studies) about the effect of NIV setting (home vs hospital) on COPD patient clinical outcome (Dretzke et al. 2016). When pooling the data of the stable population, they found that seven randomised controlled trials (RTCs) and four controlled studies all concluded that there was no significant difference in survival after 24 months between NIV settings (RCT: pooled relative risk [RR] 0.88 [0.55, 1.43], $I^2$60.4%) and controlled studies: pooled RR 1.19 [0.65, 2.18], I2=0%). Moreover, no conclusive data was shown for hospital admission/days, exacerbations not leading to hospitalisation and HRQL. In the post-hospital population, no benefits in survival were found in three RCTs (pooled RR 0.89 [0.53, 1.49], I2=25.1%) but pooling four nonrandomised controlled studies seem to reveal better survival for domiciliary NIV (pooled RR 0.45 [0.32, 0.65], I2=0%). Data on hospital management were inconsistent and HRQL assessments did not highlight any differences.

An international web-survey among physicians involved in HMV prescription for COPD patients gave valuable insight into common practise regarding HMV (Crimi et al. 2016). The most common expected benefits from placing a COPD patient on HMV is the reduction of hospital admission and improved HRQL. HMV is prescribed on average for 38.5% of patients with severe COPD. Choice of ventilation interface (oro-nasal, face mask, nasal mask or total face mask) was heterogenous as there is no clear-cut recommendation on this topic. They have all

proven effective, yet nasal mask were considered to be better tolerated. And the most common setting was the 'low intensity' approach (PSV-low) for almost half of prescribing physicians (44.4%). But it must be noted that 26.9% of prescribers used the 'high intensity' mode (PSV-High) and the more a physician prescribed NIV the more they opted for the high-intensity approach compared to 'low prescribers (29.2 ± 26.9% vs. 21.4 ± 22.7%, p = 0.04).

A German prospective study of patients (n=59) treated with IV at home aimed to determine if treatment setting impacted patient prognosis and emergency frequency (Stieglitz et al. 2017). Follow up of patients (COPD 52.5% and NMDs 37.5%) after a year showed that mortality was not impacted by treatment setting (p=0.39). Moreover, mortality rate of the invasive HMV group was negatively correlated to emergency frequency (p=0.02, CI 0.03–0.85).

A study by Schwarz et al. investigated the feasibility of HMV for COPD outpatients (n=80) (S. B. Schwarz et al. 2018a). Over half the group continued NIV without hospitalisation (64.6%; n=84) and most hospital admissions during the study were not necessary (n=93; 71.5%), only few were due to urgent issues (18.9%; n=7). Moreover, $PaCO_2$ values were better for outpatients (45.40 ± 5.27 vs. 50.05 ± 8.04, p = 0.002) as well as their SRI summary scores (55.54 ± 19.74 vs. 41.82 ± 19.59, p = 0.012).

The European Respiratory Society (ERS) has published recommendations for long-term HMV in the treatment of chronic hypercapnic COPD (Ergan et al. 2019). Although the certainty level of evidence was deemed low by the ERS, it was recommended to treat patients with stable hypercapnic COPD with long-term Home NIV (LTH-NIV). Acute home NIV was recommended following an acute episode of life-threatening COPD exacerbation. Nevertheless, if hypercapnia persisted following NIV initiation, it is recommended to implement LTH-NIV but only after titration to normalise or at least reduce $PaCO_2$ levels. And finally, the recommended initial ventilation mode for LTH-NIV should be with fixed-pressure support. Bearing in mind prescription rates vary depending on the country, COPD prevalence and rate of reimbursement (Lv et al. 2017).

A meta-analysis by Zhang et al. (5 studies, n=150) showed that the use of VAPS mode in stable COPD patients with CRF had similar efficacy performances than the standard pressure-support ventilation mode of HMV (Zhang et al. 2020a). The performance was evaluated according to ABG measurements ($PaCO_2$, PaO_2, $mSaO_2$ and $PtcCO_2$), minute ventilation and pH. Other criteria such as sleep quality (PSG, VAS, sleep questionnaire) and HRQL via SF36, SGRQ and SWT) were assessed. Once the authors removed the high weight studies, it was found that all studies showed improvement of physiological parameters for both VAPS and pressure-controlled ventilation (pH, $PaCO_2$, PaO_2, SaO_2 and $PtcCO_2$) but there was no significant different between the two groups. Sleep efficiency was slightly higher for VAPS-treated patients (p = 0.056) in one study, and another found sleep restfulness, mask fit and overall comfort level to be significantly improved for the VAPS group. Sleep questionnaires showed no statistical difference between the two groups in one trial (p = 0.142) but improved sleep efficiency after VAPS treatment in the other trial. HRQL was tested in two studies in which one found no differences between both arms after 8 weeks of treatment but the other found significant improvement in SGRQ and SF-36 emotional summary scores for the VAPS group.

A Dutch RCT compared the efficacy of home initiation of LTH-NIV in chronic hypercapnic COPD patients (Duiverman et al. 2020). The primary outcome, daytime $PaCO_2$ after 6 months compared to baseline levels, showed a significant decrease for both groups and the mean difference between study arms was 0.04kPa (5% CI −0.31 to 0. 38 kPa). Other measured parameters showed the same trend of a significant improvement for both groups after 6 months, but no notable difference between home or hospital NIV initiation: FEV1, FVC, TLC, residual volume, 6MWD, lung function, CCQ, dyspnoea and exacerbation frequency. The SRI well-being and summary scores only improved significantly for the hospital initiation group. Moreover, the initiation of NIV took substantially longer at home (14.5 days, 7-40 days) than in the hospital setting (7 days, range 4–15 days; p<0.001). A difference in the ventilation settings was reported, generally higher IPAP and EPAP in the hospital set up whereas in a home setting the IPAP was gradually increased. This seems to have had an effects on the compliance with NIV as it was better for the home group who used NIV for an average of 7.7 hours a day (±1.7 hours, median: 95% of the total number of days (range 43%–100%)) compared with 6.6 hours per day in the hospital setting (±2.1 hours use per day, median: 94% of the total number of days (range 50%–100%); p=0.037). Estimated overall costs were significantly reduced when initiating NIV at home (€3768) compared to in hospital (€8537), which can

be largely attributed to admission fees. Finally, technical problems occurred frequently during nocturnal measurements and transfer of transcutaneous gas exchange data thus, more frequent home visits were required. Nocturnal hypoventilation between both settings were comparable. The general conclusion was that home initiation of NIV was equivalent to hospital initiation additionally to freeing up hospital resources (bedspace and costs).

Raveling et al. recently published a meta-analysis (21 RCTs) to conclusively determine effects of chronic home NIV on COPD patients (Raveling et al. 2021). It was shown that patients treated with home NIV had sustainably reduced $PaCO_2$ levels after 3 months (adjusted mean difference (AMD) -0.61 kPa, 95% CI -0.77 to -0.45; 11 studies, 475 participants; high-certainty evidence) and at the 12 months follow up (AMD -0.42 kPa, 95% CI -0.68 to -0.16; 4 studies, 232 participants; high-certainty evidence). However, PaO_2 was only reduced at 3 months (AMD -0.10 kPa, 95% CI -0.65 to 0.45; 3 studies, 234 participants; low-certainty evidence), no significant difference was reported after 12 months (-0.27 kPa, 95% CI -0.86 to 0.32, 3 studies; 170 participants; low-certainty evidence). HRQL criteria seemed unchanged by HMV at both follow up timepoints (3 months: SMD 0.25, 95% CI -0.01 to 0.51; 2 studies, 219 participants; very low-certainty evidence; 12 months: SMD 0.25, 95% -0.06 to 0.55; 2 studies, 164 participants; very low-certainty evidence). And finally, mortality rates did not improve (AHR 0.97, 95% CI 0.74 to 1.28; 2 studies, 317 participants; low-certainty evidence) although admission free-survival was significantly increased after LTH-NIV (AHR 0.71, 95% CI 0.54 to 0.94; 2 studies, 317 participants; low certainty evidence). The authors concluded that NIV is indeed beneficial to COPD patients with daytime chronic hypercapnia as it lowers $PaCO_2$, increases admission-free survival and also seems to have short-term HRQL benefits.

A meta-analysis of 5 RCTs (n=419) aimed to examine the effects of LTH-NIV on COPD outpatients (X. He et al. 2021a). The authors reported that the frequency of exacerbations significantly decreased when receiving home NIV (weighted mean difference (WMD) −1.74, 95% CI: −2.90 to −0.57, P=0.004). Nevertheless, other key outcome measures where not statistically different between the control therapy group and home NIV, such as mortality rate, PaO_2, $PaCO_2$ and pH.

A recent Portuguese cross sectional multicentric study (15 centres, n=569) by Ribeiro et al. detailed the current practises in HMV for COPD patients as well as a detailed account of patients typology (Ribeiro et al. 2021). The most common evaluation criteria used to justify HMV initiation was a daytime $PaCO_2$ (50-54 mmHg) with at least two exacerbations with hypercapnic respiratory failure. It was shown that smoking history does not seem to influence HMV performance. However, patients with higher BMIs (≥ 30 kg/m²) used HMV for a longer length of time, had less severe airflow obstruction and required higher EPAP and lower pressure support. Spontaneous timed mode was the most used (92.3%) and oronasal masks were the most common breathing interface (91.7%) for HMV. Moreover, the patients with the highest HMV daily use had been on HVM for longer than 6 months, had higher ventilation pressure and lower $PaCO_2$. The authors concluded that patient population using HMV are heterogenous and many sorting criteria made it difficult to define which population benefits the most from HMV.

In summary, the practise of HMV in COPD patients tends to show improved HRQL, $PaCO_2$, exacerbation rates and admission-free survival. HMV has proven to be as safe as classical in-hospital MV and at lower costs. The initiation of NIV at home takes longer than in hospital but it leads to lower IPAP and EPAP ventilation settings. Both pressure- and volume-control ventilation are effective for COPD treatment.

High-flow ventilation modes

A case report of a 73-year old COPD patient with dementia and sleep-related hypoventilation showed that HFNC therapy not only allowed for efficient delivery of needed oxygen but also aided in the weaning of this patient to HMV (Okuda et al. 2014).

Vogelsinger et al. carried out a study in which HFNC therapy was administered to normo- and hypercapnic COPD patients (n=77) compared to conventional oxygen therapy (COT) (Vogelsinger et al. 2017). $PaCO_2$ levels were significantly lower for HFNC therapy compared to the COT group ($p<0.0001$) and safety assessment showed HFNC

therapy was well tolerates by all 77 patients (no increase in residual volume, no change in total lung volume). They concluded HFNC therapy was beneficial for normo- and hypercapnic COPD patients.

A study by Pisani looked at the effects of HFNC therapy on pulmonary mechanics and breathing patterns in stable hypercapnic COPD patients (n=14) (Lara Pisani et al. 2017). $PaCO_2$ was not significantly different between HFNC therapy, NIV and low-flow oxygen therapy. Nevertheless, they reported that respiratory muscle load was reduced with NIV and HFNC therapy compared to low flow ventilation which in turn led to an increasing expiratory time (Te) and reduced RR. They recommend using HFNC therapy over NIV as it is more comfortable for patients as the airflow is humidified and heated and the breathing interface seem better adapted.

A crossover study by Longhini et al. on COPD patients with acute respiratory failure compared NIV, COT and HFNC (n=30) (Longhini et al. 2019). Results were similar between therapies for pH ($p = 0.114$), $PaCO_2$ ($p=0.153$), Diaphragm Displacement (DD) ($p=0.875$) and diaphragm thickness at end-expiration ($Thick_{exp}$). Standard Oxygen therapy proved better for diaphragm thickness at end-inspiration ($Thick_{insp}$) ($p<0.001$), diaphragm TF ($p<0.001$), and RR ($p<0.001$ vs HFNC ; $p=0.003$ vs NIV2 ; $p=0.006$ vs NIV3) in comparison to HFNC therapy and NIV. Nevertheless, overall comfort was better reported for HFNC therapy ($p=0.004$ vs standard oxygen ; $p<0.001$ vs NIV).

A systematic review (5 studies, n=198) detailed the effects of HFNC therapy on patients suffering from exacerbated COPD (L. Pisani et al. 2019). The median initial flow delivered with HFNC was 35 [28-50] L/min, then gas flow was titrated to achieve SpO_2 target of 88 to 94%. No difference of $PaCO_2$ was reported between the treatments in 4 of the 5 studies, except for one that showed a significant reduction of $PtCO_2$ after 30 minutes of HFNC therapy compared to COT (mean difference (MD) −1.4 mmHg; 95% CI: −0.6 to −2.2; $p=0.001$). RR was not reported as different between HFNC therapy and COT (20.0±1.9 vs 21.4±4 breaths/min), nor NIV (24± vs 24±3.5 breaths/min) for most studies. Although in one study a trend that HFNC therapy seemed to reduce RR after 30 minutes of therapy compared to COT (MD −2.0 breaths/min; 95% CI: −4.5 to 0.4; $p=0.099$) was reported. This lack of notable difference between HFNC and NIV was also described at 3 (21.8±4.9 vs. 21.0±6.1 breaths/min), 24 (21.8±3.8 vs. 22.6±4.7 breaths/min) and 48 hours (22.4±4.4 vs. 21.0±4.5 breaths/min) ($p=0.611$ for all datapoints). Comfort criteria such as noisiness, weight of nasal interface, oro-nasal dryness were assessed using questionnaires. HFNC therapy were considered noisier than COT by one study team but two others found contrasting results. Others studies found patients were more comfortable with HFNC therapy compared to NIV ($p=0.024$) and showed no nasal mask-associated skin lesions compared to NIV ($p=0.04$).

A review by Elshof et al. compares the efficacy of HFNC therapy at different stages of COPD: during exacerbation, during stable hypercapnia or during exercise therapy (Elshof et Duiverman 2020). A study of 108 patients with either COPD or bronchisctasis compared HFNC therapy to standard care for a year and found that the number of exacerbations was significantly lower for HFNC-treated patients (18.2 vs. 33.5 /patient, $p=0.045$) and that median first exacerbations happened later for this same group (52 vs. 27 days, $p=0.0495$). Furthermore, trends in lung function and HRQL improvement with HFNC therapy were also reported. This new therapy was well tolerated, even in cases of long-term use. Another study showed that home use of HFNC therapy in combination with classical LTOT could be greatly beneficial for COPD patients with chronic hypoxemic respiratory failure with regards to HRQL, symptoms, exacerbation numbers and exercise quality. But in COPD patients with chronic hypercapnia it was not so clear-cut whether coupling HFNC therapy with LTOT was beneficial. Indeed, sample sizes were small but HFNC therapy did seem to reduce $PaCO_2$ and improve HRQL, further investigations are still needed and authors suggested a comparison of HFNC therapy to HI-NIV. This paper also strengthens the evidence that HFNC therapy is indeed effective for patients with acute respiratory failure, such as COPD exacerbation, which has never indisputably been the case for NIV. Finally, HFNC treatment during exercise therapy increased exercise duration (10.0±2.4 vs. 8.2±4.3 min, $p<0.05$) and improved dyspnoea ($p=0.03$) compared to the low-flow oxygen therapy group.

Kopsaftis et al. compared HFNC therapy in the pre-hospital setting for AECOPD patients (n=214) to normal titrated oxygen treatment (Kopsaftis et al. 2020). HFNC mode did not decrease mortality rate, as 11 deaths were reported compared to 2 for the titrated-oxygen control group (risk ratio (RR) 0.22, 95% CI, 0.05 to 0.97). Other

measures such as ABG, QoL, lung function or dyspnoea did not yield any significant results as confidence intervals were wide.

A trial focusing on HFNC therapy comparison to classical NIV for treatment of COPD exacerbation highlighted that although both treatments were effective in terms of RR, O_2 saturation and dyspnoea Borg score; NIV-treated patients had better mortality and tracheal intubations rates as well as shorter ICU stays (Rezaei et al. 2021). Nevertheless, NIV efficacy is limited for unstable patients unable to properly cough or with face traumas. HFNC therapy can limit respiratory resistance, inspiratory effort, dilute respiratory secretion which overall improves patient comfort. Thus, this paper confirms the efficacy of both treatments but determines that HFNC is most effective in serious acute respiratory failure, where NIV might not be as appropriate.

The use and safety of HFNC therapy in AECOPD has been assessed in a systematic review and meta-analysis (33 studies and n=492) by Yang et al. (Yang, Yu, et Chen 2021). Firstly, the risk of mortality (three studies, RR 0.91, 95% CI 0.46 to 1.79, p=0.77, very low certainty) and intubation (three studies, RR 0.94, 95% CI 0.49 to 1.78, p=0.84, very low certainty) do not seem to differ between NIV and HFNC therapy. $PaCO_2$ levels were not significantly different when comparing NIV to HFNC therapy (four studies, MD 0.24 mmHg, 95% CI: -2.24 to 2.72, p=0.85, very low certainty). This trend between NIV and HFNC therapy was also found for PaO_2 levels (two studies, MD 0.32 mmHg, 95% CI -2.50 to 3.14, p=0.82, very low certainty), pH (three studies, MD 0.01 mmHg, 95% CI -0.01 to 0.02, p=0.46, very low certainty), RR (21.8 ± 3.8 vs. 22.6 ± 4.7, p>0.05). However, it was reported that length of stay in the ICU was shorter for HFNC-treated patients in comparison to NIV-treated AECOPD patients (two studies, MD -1.49 day, 95% CI -1.88 to -1.09, p<0.0001, low certainty) and that HFNC therapy caused less discomfort compared to NIV (67.9% vs. 88.2%, p=0.008), but not in comparison to COT. Moreover, end-inspiration diaphragm thickness (median 3.7 mm, IQR: 2.9 to 4.1 vs. 4.4 mm, IQR: 3.4 to 4.9, p<0.001), thickening fraction (median 28.4%, IQR: 22.2% to 38.1% vs. 58.1%, IQR: 39.4% to 67.3%, p<0.001), diaphragm mobility during quiet breathing (MD 17.5±3.3 mm vs. 18.5±3.6 mm, p<0.01) and Diaphragmatic-rapid shallow breathing index (D-RSBI) (MD 0.51±0.20 times/(min.mm) vs. 0.41 ± 0.13 times/(min.mm), p<0.01) were all reduced after treating AECOPD patients with HFNC therapy compared to COT therapy. The evidence in this paper does seem to indicate increased performance for HFNC therapy but the robustness of the data is still lacking in order to claim this with certainty.

Another systematic review (4 RCTs and one cohort study, n=425) compared the effects of HFNC therapy versus conventional NIV therapy for patients suffering from acute type II respiratory failure ($PaCO_2$ > 6 kPa) (Alnajada et al. 2021). Comparison of NIV and HFNC therapy at various timepoints including 1h, 4h, 6h, 24h and five days after treatment initiation only showed a significant difference of $PaCO_2$ at the 4 hour follow up timepoint (1 RCT; HFNT median 6.7, IQR 5.6 – 7.7 vs NIV median 7.6, IQR 6.3 – 9.3). Moreover, for other criteria of comparison (HFNC vs NIV) such as pH (at 12 hours: MD -0.10, 95% CI -0.13, 0.06; or five days: MD -0.05, 95% CI -0.08, -0.01), PaO_2 (12 hours: MD 0.00 kPa, 95% CI −0.70, 0.70; or five days: MD −0.10 kPa, 95% CI −0.72, 0.52), mortality rate, dyspnoea score, intubation rate (3 RCTs: 2 hours: OR 0.32 95% CI 0.01, 8.02; 6 hours: OR 0.97 95% CI 0.06, 16.14; 72 hours: OR 0.33 95% CI 0.06, 1.81) there was no significant difference. When compared to low-flow oxygen therapy, HFNC therapy proved more comfortable but louder for patients.

Huang et al. published a meta-analysis (4 RCTs, n=329) also comparing HFNC therapy to COT but for patients with chronic hypercapnic COPD (Huang et al. 2021). $PaCO_2$ was the primary endpoint of comparison for HFNC treated patients (n=162) vs COT-treated patients (n=167) and no significant difference was reported MD -0.98, CI: -2.67 to 0.71, p=0.25). The secondary endpoint, PaO_2, followed the same trend with no remarkable difference between HFNC therapy and COT (MD -0.72, CI: -6.99 to 5.55, p=0.82). Although HFNC therapy has proven some efficacy in acute respiratory failure episodes such as exacerbation of COPD, the benefits in chronic failure do not seem apparent in this paper.

A Paper by Xu et al. compared the efficacy and safety of HFNC therapy to NIV in patients with COPD or acute type 2 respiratory failure (Z. Xu et al. 2021b). The significant differences between HFNC therapy and NIV therapy reported in this meta-analysis (6RCTs and 525 patients) were a notable reduction of $PaCO_2$ levels (MD = −2.64, 95% CI −3.12 to −2.15), length of hospital stay (MD = –1.19, 95 CI −2.23 to −0.05) and the incidence of nasal facial skin breakdown (odds ratio (OR) = 0.11, 95% CI 0.03–0.41). The less significant data involved PaO_2 (MD = 2.92,

95% CI − 0.05 to 5.90), intubation rate (OR = 0.74, 95% CI 0.34–1.59) and mortality (OR = 0.77, 95% CI 0.28–2.11). Based on their findings, the authors recommend HFNC therapy for acute respiratory failure and stable COPD but do recognise the data needs to be strengthened.

To summarise, HFNC therapy can be administered in COPD patients with acute or chronic respiratory failure. This new therapy is considered more comfortable and allows more efficient oxygen delivery. It was also reported that ICU stay length were shorter and PaO_2 levels improved. HFNC therapy has been coupled to conventional oxygen therapies which yielded promising preliminary data such as improvement of HRQL, symptoms, exacerbation numbers and exercise quality. But other studies found no significant physiological effect on COPD patients, data strength is still lacking.

In the treatment of OHS

A prospective study by Lucas-Ramos et al. observed OHS patients for a year (n=13), treated with BiPAP positive airway pressure ventilator for at least 4 hours a day during sleep period at home (de Lucas-Ramos et al. 2004). They reported improved $PaCO_2$, ABGs, respiratory function and ventilatory response to hypercapnia. Although the occlusion pressure (P0.1) increased for all patients, they reported a reduced response to hypercapnia. Their data suggests that nocturnal non-invasive HMV seems to promote the recovery of the respiratory centre's sensitivity, which would explain why even daytime gas measures were improved.

Palm et al. studied gender differences between long-term HMV patients in Sweden between 1996 and 2004 (Palm et al. 2016). The comparison of 1527 patients with OHS found that improvement of blood gases and survival rates were comparable between genders. A one-year follow up of patients reported a mean $PaCO_2$ reduction of 1.2 kPa. OHS patients had higher Epworth Sleepiness Scale (ESS) scores than patients treated with long-term HMV for other disorders.

Soghier et al. published a systematic review in which they compare NIV and CPAP ventilation modes for the treatment of OHS (Soghier et al. 2019). The data of 3 randomised trials, one observational study and one long-term follow up were compiled and compared. Mortality rates were similar between NIV and CPAP-treated patients (11% vs. 14.9%; RR, 0.82; 95% CI, 0.36–1.87) in the study with long-term follow up (5.5 years) but also for the observational study (5% vs. 4.8%; RR, 1.04; 95% CI, 0.31–3.46). However, the data lacks robustness given the large CIs and low certainty. The resolution of hypercapnia ($PaCO_2 \leq 45$ mmHg) after NIV and CPAP therapy was equally successful for both treatments after a 3 month follow up (46.6% vs. 36.3%; RR, 1.29; 95% CI, 0.94–1.77) and a 3 year follow up (51.9% vs. 40.7%; RR, 1.28; 95% CI, 0.91–1.79). Daytime PaO_2 measures show significant improvement in the short- and long-term but no remarkable difference between NIV and CPAP (3 months follow up: MD, 20.21 mm Hg; 95% CI, 23.52 mm Hg to 13.1 mm Hg; and 3 year follow up: MD, 21.80 mm Hg; 95% CI, 24.92 mm Hg to 11.32 mm Hg). The same interpretation can be observed for daytime $PaCO_2$ levels where NIV versus CPAP showed no significant difference after 3 months (MD, 21.08 mm Hg; 95% CI, 22.91 to 10.76 mm Hg) and 3 years (estimated MD, 20.67 mm Hg; 95% CI, 22.16 to 10.82 mm Hg) of therapy. Sleep was assessed using the AHI, ESS and sleep quality with the Pittsburgh Sleep Quality Index. Overall, improvement in sleep quality was equally significant with either NIV or CPAP therapy. Nevertheless, a slightly better improvement of sleep quality was reported using the Pittsburgh Sleep Quality Index for NIV compared to CPAP (MD, 13.67 points; 95% CI, 11.25 to 11.69 points). But it must be mentioned the certainty of this data is very low due to high risk bias and imprecision. HRQL is significantly enhanced for both methods of home ventilation but not one was notably better than the other after 3 months or 3 years of therapy. And even though there was a slightly better improvement of physical capacity, measured by the 6-minute walk distance test at 2 months for NIV therapy, in the long term no difference was significant. After 3 years of either treatment a marked reduction of dyspnoea was reported. Other aspects of the patients life such as the number of hospital or emergency room visits were tracked and no significant difference between NIV and CPAP groups at 3 months (9.7% vs. 10.3%; RR, 0.94; 95% CI, 0.20 to 4.27) nor 5.5 years (52.6% vs. 44.9%; RR, 1.17; 95% CI, 0.88 to 1.55) were observed. After comparing all of the data, it was advised to preferentially suggested CPAP before NIV for stable ambulatory OHS patients as there is no notable medical difference between the two therapies. Nevertheless, NIV is substantially more expensive and requires more resources than CPAP.

A multi-centre interventional trial by Arellano-Maric et al. compared different HMV modes (NIV vs CPAP) for the treatment of 42 OHS patients (Arellano-Maric et al. 2020). Moreover, they also tested an auto-adjusted CPAP (APAP) device under PSG as a titration method. Among the patients switched to CPAP HMV, for a median of 35 days, 71% (95% CI: 55–84%) maintained a daytime $PaCO_2$ level ≤ 45 mmHg. 84% (95%CI: 67–95%) of patients with acceptable APAP response following titration maintained daytime $PaCO_2$ levels of ≤ 45mmHg. No deterioration of polysomnographic parameters, HRQL (SRI questionnaire) or respiratory functions were reported after the switch to CPAP therapy. It was shown that CPAP restores normocapnia for some patients. Nevertheless, some patients with higher BMIs (mean: 47.1±10 vs 43.9±6.4 kg/m²), are CPAP non-responders due to mild hypercapnia (mean: 47.9±2.7 mm Hg). In fact, this group of patients required slightly higher CPAP than the CPAP success group (mean: 15±2.3 vs 13.6±1.6 mbar). 24 of the 37 patients included in the study preferred CPAP as their long-term ventilation therapy and gave better scores for CPAP therapy in 5 out of 7 HRQL questionnaires.

In summary, nocturnal HMV can improve $PaCO_2$, ABGs, respiratory function and response to hypercapnia. OHS patients had higher ESS scores than patients treated with long-term HMV for other disorders. It is recommended to start OHS ventilation treatment in CPAP mode for stable ambulatory OHS patients.

In the treatment of NMDs

QoL of patients with NMDs treated with HMV was assessed by Markström et al. (Markstro¨m et al. 2002). HRQL was evaluated using three widely accepted HRQL questionnaires: the Sickness Impact Profile (SIP), the Health Index (HI) and the Sense of Coherence (SOC) Scale. The higher these scores are, the better the perceived health by the patient. A comparison of home invasive- vs home NIV showed higher overall HI scores for IV (27.8±3.7 vs 25.2±3.6) but no significant difference was reported when using the SOC scale or SIP. And comparison of the three main diagnostic groups (scoliosis, postpolio dysfunction and NMD) treated with NIV showed no difference when using the HI or SOC scale. However, the SIP questionnaire found that patients with postpolio dysfunction scored less in the psychological dimension indicating depression.

A study by van den Biggelaar et al. aimed to compare HMV initiation in a hospital setting versus at home via telemedicine for patients with a NMD or a CWD (van den Biggelaar et al. 2020). Indeed, nowadays it is common practice to firstly start HMV therapy in hospital which consumes resources such as bed space, hospital funds and healthcare professional time which can all delay HMV initiation. Among the total 96 patients (n=49 hospital group vs n=47 home group), the predominant diagnosis was ALS, diaphragm paralysis and MD. The primary outcome was transcutaneous measure of daytime $PaCO_2$ after 6 months of treatment which significantly improved for both groups, but no notable difference between the two arms was reported. The same was concluded for nocturnal transcutaneous $PaCO_2$ levels. Other factors were taken into accounts such as HRQL assessment via multiple questionnaires (SRI and HADS). Although patients showed improved scores over the first 6 months of treatment for both questionnaires, they did not differ depending on the initiation context. Costs analysis (absolute costs and costs relating to the EuroQol-5Dimensions questionnaire (EQ-5D) and Dutch reference healthcare prices) showed an average saving of €3225 (95% CI: 4279 to 2107) per patient who had HMV initiated at home due to reduced hospital admissions.

Overall, invasive HMV patients showed better HRQL scores (HI) than other NMD patients. Initiation of HMV at home or in hospital did not yield any notable difference in daytime $PaCO_2$ nor HRQL after 6 months. Only costs were significantly lower in home-initiation, average saving of €3225 per patient.

In the treatment of various chest wall malformations

A randomised trial by Pallero et al. determined if the setting (hospital or ambulatory) of HMV initiation was impactful on patients or costs (Pallero et al. 2014). Among the 53 HMV-treated patients, most had restrictive thoracic deformities (547%; n=29), others had NMDs (28.3%; n=15) or OHS (17.0%; n=9). Moreover, 27 underwent ambulatory adaptation (AA) and 26 hospital adaptation (HA). For both groups, the $PaCO_2$ levels significantly decreased compared to the baseline after 1 month (AA vs HA, 5.29 mmHg with reduction 2.9 mmHg; 95% CI 1.0-4.8 vs 5.49 mmHg with reduction 2.8mmHg; 95% CI 0.9-4.6; p=0.9176) and 6 months (AA vs HA, 4.9

mmHg; 95% CI 2.3-74 vs 3.3 mmHg; 95% CI 1.4-5.1). Between both groups $PaCO_2$ did decrease more for the AA group (difference 1.6 mmHg; 95% CI 4.6 to -1.5). No other measures (HRQL, compliance, scheduled visits, exacerbation, emergency room admissions, hospital admission, ICU admissions) showed a significant difference between adaptation groups. Finally, costs assessments showed an initial big difference between the AA (1500€) and HA (2692€) mainly linked to initiation admission costs (AA 541€ vs HA 1886€), but at the follow up timepoint the gap had narrowed (AA 960€ vs HA 806€).

The treatment of acute respiratory failure or COVID-19 via high-flow nasal cannula oxygen therapy or c-flow

High-flow ventilation modes

A systematic review (3 RCTs) by Algamdi et al. aimed to establish the role that HFNC therapy can play in patients with AHRF (Algamdi et Ball 2016). Overall, they did not report a significant effect of HFNC therapy on treatment failure (need for intubation, ventilation mode change or HFNC therapy discontinuation) compared to NIV and other conventional therapies. But they did highlight that among patients with the most severe AHRF, treatment failure was significantly lower (p=0.01). The authors consider the data to be of low certainty and needs to be confirmed with further studies.

In 2020, amidst the worldwide SARS-CoV2 (COVID-19) pandemic, the WHO commissioned reviews regarding HFNC-based treatments (Agarwal et al. 2020). This work was divided in two separate reviews, the first (12 RCTs; n=1989) aimed to evaluate the safety and efficacy of HFNC therapy in COVID-19 patients; the second (4 studies) assessed the risk of droplet dispersion and thus transmission during this therapy. Reports are that HFNC therapy seemingly reduces the need for IV (relative risk, 0.85; 95% CI, 0.74 to 0.99) and escalation of oxygen therapy (RR, 0.71; 95% CI, 0.51 to 0.98) for patients with respiratory failure. There was notable difference in terms of mortality or length of time spent in ICU. However, new adverse events were identified in this paper: heat-related discomfort and thoraco-cervical discomfort were all considered common for HFNC therapy. The second review had mixed results regarding droplets dispersion. The two simulation studies demonstrated no additional dispersion but another reported flow rate increase was correlated with higher droplet dispersion. It must be noted that none of the data presented involves COVID-19 patients but patients with AHRF and is generally of a low certainty level.

In a letter to the editor, Brusasco et al. reported their use of CPAP during the first weeks of the COVID-19 pandemic in Italy in 2020 (Brusasco et al. 2021). They suggest using CPAP for AHRF but also report that use of high-flow ventilation must be used with caution as it could be harmful for patients.

Efficacy and safety of HFNC therapy (≥ 20 L/min airflow) in ICU patients suffering from respiratory failure was reviewed (31 RCTs, n=5136) by Lewis et al. (Lewis et al. 2021). The authors found that HFNC therapy seemed to lead to less treatment failure although evidence was considered of low certainty. There was also no clear-cut evidence that outcome measures such as mortality (RR 0.92, 95% CI 0.64 to 1.31; 5 studies, 1758 participants; I2 = 44%; low-certainty evidence), length of hospital/ICU stay (MD -0.72 days, 95% CI -2.85 to 1.42; 2 studies, 246 participants; low-certainty evidence), comfort scores (MD 1.33, 95% CI 0.74 to 1.92; 2 studies, 258 participants) and RR differed between HFNC and COT. But HFNC therapy did improve the PaO_2/FiO_2 ratio for up to 24 hours (MD -58.10 mmHg, 95% CI -71.68 to -44.51; 3 studies, 1086 participants; low certainty evidence).

Ogawa et al. published a review in order to assess evidence around different COVID-19 treatments, including HFNC therapy (Ogawa et al. 2021). Before the COVID-19 pandemic, HFNC therapy was already used in cases of AHRF. However, the benefits of HFNC compared to NIPPV was never completely confirmed. Amid the pandemic, a small-scale study conducted on COVID-19 patients in China showed HFNC therapy significantly improved oxygenation (PaO_2/FiO_2 ratio) after 72h compared to COT (321±5 vs. 286±7, p=0.001) but did not change ICU length of stay (4.0 0.7 vs. 4.9 1.0 days, p=0.24). Moreover, other studies have highlighted a possible reduction of intubation rates with HFNC therapy but no difference in mortality rates. The authors suggest that HFNC therapy could be an affective therapeutic strategy of oxygenation for COVID-19 patients with respiratory failure but that the data needs to be strengthened with further studies. Additionally, the spread and transmission of the virus to healthcare workers seems very limited as long as they wore the appropriate face masks (N95/FFP2) in a negative pressure room.

A recent systematic review and meta-analysis (9 studies, n=1582) by He et al. compares the performance of HFNC therapy and NIV for the treatment of COVID-19 (Y. He et al. 2022). There was no notable difference between NIV and HFNC therapy in terms of incidence of invasive MV (five studies; p=0.71) and length of stay in the ICU (seven studies; p=0.33). However, less patients treated with HFNC had died after 28 days (five studies; p=0.0005), length of hospital stay was shorter (four studies; p<0.05) and the oxygenation index (PaO_2/FiO_2) was significantly improved after 24h in the HFNC group compared to the NIV group (p<0.00001). The authors concluded that the use of HFNC therapy is recommended in COVID-19 but it must be with caution and careful monitoring as the data shown in this meta-analysis is still weak and needs further consolidation.

Xu et al. published as meta-analysis (25 studies, n=2851) regarding the effectiveness of HFNC therapy to treat COVID-19 and predictive factors of treatment failure (Y. He et al. 2022). The authors suggest HFNC therapy is an effective therapy for COVID-19 patients with AHRF. Although there is a trend suggesting HFNC therapy could lower mortality and intubation rates, this has not always been clear-cut especially when comparing to COT or NIV. The failure of HFNC therapy was associated with older age, higher BMI, sequential organ failure assessment (SOFA) and Acute physiology and chronic health evaluation (APACHE) II scores, RR, heart rate and lower PaO_2, SpO_2, PaO_2/FiO_2 and ROX index (p<0.05 for all). Smokers and patients with other comorbidities (hypertension, coronary artery disease, diabetes, COPD, chronic kidney disease and malignancy) also showed less success rate (p<0.05 for all).

To summarise, in the most severe cases of acute respiratory failure, HFNC therapy seems to significantly lower treatment failure (*ie.* need for intubation, ventilation mode change or HFNC therapy discontinuation). COVID-19 patients treated with HFNC therapy seem to have a reduced need to IV and improved oxygenation (PaO2/FiO2 ratio) for up to 24 hours after initiation. But there was no difference in mortality, RR, nor length of stay in the ICU compared to conventional treatments. The use of HFNC therapy for acute respiratory failure still needs to be further tested.

3.10.4.7 Patient benefits

No direct patient benefits associated only to the ventilator were described in the literature. Indeed, the benefits reported relate to the ventilation therapy – *i.e.* the gas/air blend delivered to the patient in association with the ventilator.

Nonetheless, the larger picture is that HMV has patient benefits that are applicable to the whole system and mentioned here to contextualise to how HMV benefits patients when compared to hospital ventilation:

- *In the treatment of COPD*
  - **Classical ventilation modes**
    - Offer adequate treatment of COPD with low-risk intervention (Stieglitz et al. 2013)
    - Improved survival (Dretzke et al. 2016; F. M. Struik et al. 2014)
    - Improved $PtcCO_2$ (F. M. Struik et al. 2014; Zhang et al. 2020a)
    - HRQL improvement (Majorski et al. 2021; S. B. Schwarz et al. 2018b; F. M. Struik et al. 2014; Zhang et al. 2020a)
    - No difference in mortality compared to NIV in-hospital set up (S. B. Schwarz et al. 2018b)
    - Improved $PaCO_2$ levels (Raveling et al. 2021; S. B. Schwarz et al. 2018b)
    - Better overall therapy comfort (Zhang et al. 2020a)
    - Improved respiratory compliance for HMV initiation at home (Duiverman et al. 2020)
    - Considerable costs reduction (Duiverman et al. 2020)
    - Decrease of exacerbation frequency (X. He et al. 2021b)

  - **High-flow ventilation modes**
    - Improved $PaCO_2$ levels (Alnajada et al. 2021; Vogelsinger et al. 2017; Z. Xu et al. 2021b)
    - Treatment better tolerated (Vogelsinger et al. 2017)
    - Respiratory muscle load reduction (Vogelsinger et al. 2017)
    - RR decreased (Vogelsinger et al. 2017)

- More comfortable (Alnajada et al. 2021; Longhini et al. 2019; L. Pisani et al. 2019; Rezaei et al. 2021; Vogelsinger et al. 2017)
- Improved $PtcCO_2$ (L. Pisani et al. 2019)
- Decrease of exacerbation frequency (Elshof et Duiverman 2020; Huang et al. 2021)
- Length of stay in ICU (Yang, Yu, et Chen 2021)
- Reduction of end-inspiration diaphragm thickness (Yang, Yu, et Chen 2021)
- Thickening fraction reduction (Yang, Yu, et Chen 2021)
- Reduction of diaphragm mobility during quiet breathing (Yang, Yu, et Chen 2021)
- Diaphragmatic-rapid shallow breathing index decrease (Yang, Yu, et Chen 2021)
- Shorter stay in hospital (Z. Xu et al. 2021b)
- Lower incidence of nasal facial skin breakdown (Huang et al. 2021, 221)

- *In the treatment of OHS*
  - Recovery of respiratory centre sensitivity (de Lucas-Ramos et al. 2004)
  - Improved $PaCO_2$, ABGs, respiratory function and ventilatory response to hypercapnia (de Lucas-Ramos et al. 2004)

- *In the treatment of NMDs*
  - Initiation at home is more cost-effective (Biggelaar et al. 2020)

- *In the treatment of chest wall deformities*
  - At-home HMV initiation improves $PaCO_2$ levels (Biggelaar et al. 2020; Pallero et al. 2014)
  - HMV is cost-effective (Pallero et al. 2014)

- *In the treatment of COVID-19 via high-flow oxygen therapy*
  - Reduces the need for IV (Agarwal et al. 2020)
  - Improved oxygenation (PaO_2/FiO_2 ratio) (Ogawa et al. 2021)
  - Lower morality (Y. He et al. 2022)
  - Efficient patient triage with identification of factors associated to treatment failure: older age, higher BMI, SOFA and APACHE II scores, RR, heart rate and lower PaO_2, SpO_2, PaO_2/FiO_2 and ROX index (Y. He et al. 2022)

3.10.4.8 Contra-indications

In light of the increasing use of HMV, this type of therapy is applied in many respiratory disorders (HAS, recommendations for HMV in NMDs 2006; Koblizek et al. 2013; Macrea et al. 2020; Rabec et al. 2016; Wedzicha et al. 2017). But as there are no clear-cut undisputed recommendations there are also no firm contraindications; this also applies for HFOTs (Nishimura 2016). The only contraindication was patient refusal or physical obstruction (Wolfram Windisch et al. 2018).

3.10.4.9 Side effects – Complications

As described for performance and benefits, the side effects reported are linked to the use of MV in general and are not specific of HMV. They are listed below:

- Abdominal distension (Pallero et al. 2014)
- Aerophagia (Duiverman et al. 2020)
- Barotrauma (Lewis et al. 2021)
- Claustrophobia (Afshar et al. 2020; Pallero et al. 2014; Sinuff, Keenan, et Department of Medicine, McMaster University 2004)
- Discomfort (Duiverman et al. 2017; Ergan et al. 2019; Kopsaftis et al. 2020; L. Pisani et al. 2019; Sinuff, Keenan, et Department of Medicine, McMaster University 2004; Z. Xu et al. 2021b)
- Dyspnoea (Lewis et al. 2021; Stieglitz et al. 2013; 2017)
- Excessive 'deventilation dyspnoea' (Duiverman et al. 2020)

- Eye irritation (Afshar et al. 2020; Nishimura 2016)
- Gastric distention (Afshar et al. 2020)
- Increase of secretion (Stieglitz et al. 2017)
- Oro-nasal dryness (Afshar et al. 2020; Duiverman et al. 2020; Kopsaftis et al. 2020; Lewis et al. 2021; Nishimura 2016; L. Pisani et al. 2019)
- Rhinitis (Afshar et al. 2020; Pallero et al. 2014)
- Skin lesion (Afshar et al. 2020; Ergan et al. 2019; Lewis et al. 2021; Mandelzweig et al. 2018; Pallero et al. 2014; L. Pisani et al. 2019; Sinuff, Keenan, et Department of Medicine, McMaster University 2004; Z. Xu et al. 2021b)
- Ventilator-induced injury (Zhang et al. 2020a)

The complications specifically linked to HFNC mode are listed below:

- Heat-related discomfort (Agarwal et al. 2020)
- Mild altered level of consciousness (Agarwal et al. 2020)*
- Thoraco-cervical discomfort (Agarwal et al. 2020)

Mild altered level of consciousness: The manufacturer does not consider this side effect to be directly related to HFNC therapy but rather the illness itself (ie. COVID-19). Thus, this risk shall not be added to the risk analysis file nor the IFU. Nevertheless, during all future updates this specific side effect shall be carefully monitored in the literature and added to the appropriate document if deemed necessary.*

All of the above mentioned side effects are mild to moderate in nature and manageable; they are far outweighed by the benefits of HMV.

Moreover, the increasing number of patients needing HMV is causing a strain on healthcare systems as it requires resources, trained and available medical staff to properly care for patients. Prevalence of HMV can depend on factors such as country income, population typology and culture. A study of HMV use in New Zealand and Australia found the most common indication for HMV was OHS, unlike most countries in Europe (COPD) (Garner et al. 2013). Furthermore, a lack of precise national and international guidelines partly explains the heterogeneity of HMV practises. It must also be noted that prescription rates can significantly vary depending on the location, size and experience of the healthcare centre as well as the physician (Laub et al. 2004).

A data search via the FDA Total Product Life Cycle (TPLC) database was performed on 21st March 2022:

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfTPLC/tplc.cfm

The search terms used were “home ventilator”:

- “*Continuous, Ventilator, Home Use*”: code NOU and regulation number: 868.5895
  Definition: This product code was needed for the home use indication. CBK (“Ventilator, Continuous, Facility Use“) is a device meant for use in medical centres, and NOU is a device intended for home use.

- “*Ventilator, Continuous, Minimal Ventilatory Support, Home Use”*: code NQY and regulation number: 868.5895
  Definition: This continuous ventilator, which operates using a fixed or passive exhaust port, is intended to treat patients with respiratory failure in the home.

Limits

- Medical devices
- Since 2007

The following table summarises the 5 most common problems encountered for the device and the patients

Table 33: Three (3) most common side effects-complications reported for home mechanical ventilators.

	Device problems	Patient problems
"*Continuous, Ventilator, Home Use*": code NOU	Device displays incorrect message	No Consequences Or Impact To Patient
	Battery problem	No clinical signs, symptoms or conditions
	Failure to calibrate	No patient involvement
	Protective Measures Problem	Insufficient information
"*Ventilator, Continuous, Minimal Ventilatory Support, Home Use*": code NQY	-	-

None of the complications reported in the TPLC database had an impact on patient health.

3.10.4.9.1 Hazards related to substances or technologies

No specific hazard due to substances or technologies was identified for the use of HMV in the studies included in this section.

3.10.4.9.2 Divergent opinion among professionals

The benefits of NIV for patients with acute or chronic respiratory failure was long debated as no high-quality robust data was yet published (Hannan et al. 2014; Fransien M. Struik, Lacasse, et al. 2013). Recently, more strong data has been published, which confirms what physicians saw first-hand in practice (Coleman, Wolfe, et Kalhan 2019; Majorski et al. 2021; Raveling et al. 2021). The safety and performance of NIV in a home setting was next to be confirmed (Comer, Oakes, et Mukherjee 2015; Ergan et al. 2019; X. He et al. 2021a; F. M. Struik et al. 2014; Suh, Murphy, et Hart 2019b; Vitacca et al. 2009).

Nevertheless, the typology of patients that will benefit the most from HMV is still not completely clear and must be better defined (Coleman, Wolfe, et Kalhan 2019; P. B. Murphy et Hart 2014). This is in part due to a lack of consensus around which evaluation criteria are the most important for patient assessment as a wide range of disorders can lead to ventilation needs (eg physiopathological measures vs QoL outcome measures) (Majorski et al. 2021). Indeed, although HRQL is deemed an important benefit for patients, HRQL questionnaires are not consistently carried out before NIV initiation.

Moreover, NIV is not started purely based on hypercapnia as this is not clearly demonstrated as a cause of mortality (Raveling et al. 2018). Although recent work has highlighted the possible prognostic value of $PaCO_2$ in LT-NIV COPD patients (Crimi et al. 2016).

3.10.4.9.3 Unmet medical need

Questions of inequality of access to HMV, or even long-term ventilation in general, have been raised. A comparison of upper middle-income and high-income countries does not seem to show a difference in mortality and in NIV failure rates. Unfortunately, data regarding low-income countries is not sufficiently robust to be confidently compared to higher-income countries. Indeed, this could be linked to the lack of NIV use, lack of data and a lack of publications (Mandelzweig et al. 2018).

3.10.4.9.4 Summary table of the performance and safety data retained on HMV

Twenty nine (29) articles were selected to support the performance and safety of HMV. Indeed, performance and safety of home mechanical ventilators cannot be separated from the whole system that includes the home mechanical ventilator, tubing, masks or cannulas. This explains why, in the articles included, only the performance and safety of artificial ventilation is described as opposed to that of ventilators. Nonetheless, the data found on HMV is summarised in the following table:

Table 34: Summary table of performance and safety data retained for HMV

Ref. & Type of study	Population & Indication	Therapy	Aim	Evaluation criteria	Results
(Markstro¨m et al. 2002) Retrospective study	91 adult patients: postpolio dysfunction (n=33; 37%), NMD (n=16; 20%), scoliosis (n=13; 15%), and other various diagnoses (n=29; 28%).	HMV	Assessment of HRQL of HMV patients with NMDs or skeletal deformities using different questionnaires.	The SIP, the HI and SOC scale, ventilation interface (invasive vs noninvasive).	Overall, patients treated with HMV had good perception of their health. Patients with IV (tracheostomy) reported higher HI scores than the NIV group. In NMD patients, IV groups scored better in the SIP. Women showed better SIP scores than men.
(Wolfram Windisch et al. 2003) Protocole validation study	226 patients with chronic respiratory failure: COPD (n=78), idiopathic kypho-scoliosis (n=57), NMD (n=49) and post-tuberculosis sequelae (n=20), OHS (n=12) poliomyelitis sequelae (n=4), phrenic nerve lesion (n=3) and central hypoventilation syndrome (n=3)	HMV	Development of the SRI questionnaire to better assessed HMV patients' HRQL.	SRI compared to SF-36, lung function parameters, inspiratory mouth pressures and ABG measurements.	Highly reliable and multidisciplinary results of the SRI scores. Higher discriminatory validity than SF-36 questionnaire, new possibility to take into account diagnostics in HRQL assessment for CRF patients.
(Chu et al. 2004) Multi-centre retrospective study.	249 patients: COPD with chronic hypercapnic failure (n=121, 48.6%), RTDs (n=85, 34.1%), complicated obstructive sleep apnoea (OSA) (n=43, 17.3%).	HMV, bi-level pressure-support ventilators (not specified)	Description of HMV use, survival and predictors of death in Hong Kong.	Primary HMV indication, HMV continuation rate at 36 months	The predominant mode of HMV was NIV by bilevel pressure support ventilators (n=236). Just under half of the patients were treated for COPD (48.6%) and 66.2% were still using HMV after 3 years of treatment.
(Schönhofer et al. 2006)	25 patients with HRF and COPD (NIV)	HMV BiPAP-ST T; Respironics; Murrysville, PA	To evaluate the effect of noninvasive HMV on inspiratory muscle strength in COPD patients.	Spirometry and body plethysmography, daytime blood gases, maximal statis inspiratory mouth pressure (PI_{max}), maximal expiratory pressure (PE_{max}), transdiaphragmatic pressure (Tw Pdi) measured by using oesophageal pressure	Tw Pdi is not increased as a results of NIV and low-frequency diaphragm fatigue is not present in patients prior to therapy.

Ref. & Type of study	Population & Indication	Therapy	Aim	Evaluation criteria	Results
				(P_{eos}) and gastric balloon pressure (P_{ga}) catheters.	
(Vitacca et al. 2006) Pilot study	45 patients with CRF: COPD, NMDs (including ALS) and diffuse interstitial lung diseases.	HMV	Assess the feasibility and efficacy of HMV when it is monitored by telemedicine.	Ventilation needs (hours/day), pre-morbidity lifestyle score (PMLS), level of nursing dependency, respiratory functions, respiratory muscle pressure, ABGs (air and oxygen), dyspnoea evaluation (BORG scale) and comorbidities. Criteria evaluated during follow ups: number of respiratory exacerbation episodes, causes of exacerbations of CRF, number of ICU admissions, number of emergency admissions, number of GP calls made, number of scheduled nurse calls, numbers of call to the respiratory consultant, requests for new diagnostic examinations, problem-solving calls, problems with the ventilator, changes in ventilator setting, changes in therapy (oxygen prescription and drugs), number of home nurse visits, number of saturometric recordings and survival.	Most issues encountered by patients were solved during telemonitoring and teleassistance by nurses only (86%), or nurses and respiratory physician together (14%). HMV telemonitoring has proven feasible and the pSat recordings in particular for titration of oxygen, mechanical ventilator settings and stabilisation of relapses. The follow ups and possible modulation of HMV features can be successfully done by nurses in light of the pSat data.
(Doménech-Clar et al. 2008) Prospective study	42 patients (home n=21; hospital n=21) with restrictive ventilatory disorders (NMD or thoracic cage disorders, OHS or diaphragmatic relaxation).	HMV	Comparing HMV adaptation and follow up in an ambulatory versus a hospital setting.	Borg scale (dyspnoea), respiratory function, ABGs, nocturnal pulse oximetry, HRQL questionnaire (SF-36).	Borg scale and nocturnal pulse oximetry were similarly improved for both groups, no difference between groups. Although both groups saw an improvement of PO_2 and PCO_2 levels, the ambulatory group reported significantly higher values (PO_2, P=0.033; PCO_2, P=0.020). SF-36 analysis using Student's t-test showed higher improvement of general health for the ambulatory group at 6 months post-HMV (p<0.02).

Ref. & Type of study	Population & Indication	Therapy	Aim	Evaluation criteria	Results
(López-Campos et al. 2008) Observational cross-section study	115 adult patients receiving noninvasive HMV: OHS (n=37), thoracic cage abnormalities (n=33), NMD (n=18), COPD (n=15) and sequelae of tuberculosis (n=12)	HMV	Evaluate HRQL of patient treated with noninvasive HMV.	Spanish version of the SRI questionnaire, socio-demographic factors (including, gender, age and level of education), employment status, extend of smoking history, primary diagnosis and comorbidities (Charlson-Age Comorbidity Index) and measure of dyspnoea.	This study founds factors that are good predicators of HRQL: (1) dyspnoea, being the most prominent predictor, (2) an obstructive pattern on PFT, (3) the number of hospitalisations and (4) the number of emergency room admissions in the last year.
(W. Windisch 2008)	85 patients: COPD (n=27), RTD (n=29), (n=17), OHS (n=9) and other (n=3)	HMV	Assessment of the advantages and difficulties of HMV.	Day and night time blood gases and lung function measures, PI_{max}, SF-36 and SRI questionnaires as well as physical component summary (PCS) and mental component summary (MCS) were used for HRQL assessment.	HMV seems to improve HRQL for all conditions within one month after treatment establishment, and this can be sustained for the following 12 months.
(Dogan et al. 2010)	170 CRF patients	HMV	Effect of Noninvasive MV on the health of CHRF patients.	ABG measurements and PFT, number of hospitalisations and survival.	A significant decrease in the $PaCO_2$ levels 1 year after NIMV initiation for group 1 ($p<0.05$). Survival was higher in group 1 compared to group 2 (respectively 40.27 ± 3.56 vs 27.35±3.68) ($p=0.005$). In fact, a significant positive correlation between increased NIMV usage and improved survival was reported in group 1 ($p=0.038$). No significant difference in hospital admissions nor in PFT and ABG measures were noted between the two groups.
(Racca et al. 2011) Observational multi-centre study	362 patients: NMD (n=178), chronic lung and upper respiratory tract disease (n=64), hypoxic (ischemic) encephalopathy (n=48), abnormal ventilation control (n=44), spinal cord injury (n=11), chest anomalies (n=16) and other (n=1)	HMV	To describe characteristics of long-term HMV for children in Italy.	Primary indication for long-term HMV, ventilation interface (invasive vs noninvasive) and duration of ventilatory support	The most frequent indications were NMDs, notably the most common diagnostic was spinal muscular atrophy (MSA) (n=78). Median length of HMV was one year. The most common ventilation interface was noninvasive (59%), with a higher prevalence in later infancy and adolescence. IV preferentially associated to younger patients with longer ventilation needs and generally NMDs or hypoxic (ischemic) encephalopathies.

Ref. & Type of study	Population & Indication	Therapy	Aim	Evaluation criteria	Results
(Storre et al. 2014)	10 COPD or CHRF patients already treated with HI-NIV (> 3 months)	HMV Vivo 40 or Vivo 50 ventilator (Breas Medical, Mo¨lnlycke, Sweden)	Determine the efficacy of hybrid mode using target tidal volume NIV (target V_T NIV) during HI-NIV	Nocturnal hypoventilation, daytime hypercapnia, overnight ventilation patterns, subjects' tolerance, HRQL, lung function, and exercise capability.	No clinical benefit seems added to HI-NIV by using target V_T NIV. All of the following outcome measures were unchanged by the hybrid ventilation mode: sleep quality, the control of nocturnal hypoventilation, daytime hypercapnia, overnight ventilation patterns, subjects' tolerance, HRQL, lung function and exercise capability. Nevertheless, it could offer better physiological breathing patterns with lower leakage and higher expiratory volumes.
(Huttmann, Windisch, et Storre 2015)	32 Adult patients with severe CRF: NMD (n=14), COPD (n=11), overlapping COPD and OHS (n=2), destroyed lungs (n=1) and other (n=4)	HMV	To describe details on HMV patients' living conditions and HRQL.	Primary disease, dependency on HMV, comorbidities, living situation, MV, medical and nursing care and supply of technical aid. Dependency on nursing care according to the Barthel Index of Activity of Daily Living, HRQL using the SRI Questionnaire and ventilation interface type (invasive vs non-invasive).	HRQL does not seem dependant on interface type (invasive vs non-invasive), living situation. NMD patients scored significantly higher on the SRI questionnaire due to NMD patient being typically younger and having less comorbidities that older patient with chronic lung disease. Longer survival rate for chronic lung disease patients than NMD patients. Many patients in the study show a high SRI score showing HMV can be associated to a very good HRQL.
(MacIntyre et al. 2016) SR 1 RCT and 25 Observational studies	4425 patients: (NMD) (n=1697), RTD (n=481), OHS (n=293), and other (n=748)	HMV	Evaluating HMV for non-COPD patients with CRF, in terms of HRQL	- Primary outcome: HRQL measured by a validated HRQL assessment tool and hospitalisation requirements - Secondary outcome: family caregiver (FCG) burden (defined by validated questionnaires), costs for either the families or the health system, sleep quality and incidence of decannulation.	This review suggests that patient with CRF linked to NMD, RTD and OHS have improved QoL and reduced hospitalisation needs. Caregiver burden associated with HMV was generally high; however, it is poorly described.

Ref. & Type of study	Population & Indication	Therapy	Aim	Evaluation criteria	Results
(P. B. Murphy, Arbane, Bisquera, et al. 2017; P. B. Murphy et al. 2011; 2016; P. B. Murphy, Arbane, Phillips, et al. 2017) Randomised controlled trial *UK HOT-HMV trial*	116 COPD patients: (n=59) HOT group and (n=57) HMV group	HMV	Comparing Home Oxygen therapy (HOT) to HMV	- Primary outcome: Anthropometrics, ABGs, HRQL, lung function, death rate, dyspnoea level and sleep quality - Secondary outcome: all-cause hospital admissions and exacerbation rate at 12 months	- Both methods improve ventilation compliance and sleep quality. - Significantly improved criteria for the HOT+HMV arm include: median time to readmission, overall hospital admission rate, 12 month exacerbations, $PACO_2$ and dyspnoea. - No significant difference on overall HRQL
(Povitz et al. 2018) Retrospective cohort study	Thoracic cage restriction diseases (kyphoscoliosis (n=51), fibrothorax (n=117), thoracoplasty (n=9), obesity (n=743), thoracic resection (n=14)) and NMDs (ALS (n=350), muscular dystrophy (n=317), diaphragmatic paralysis (n=37), myasthenia gravis (n=294), Guillain–Barre´ syndrome (n=9), spinal cord injury (n=247), stroke/transient ischemic attack (n=51), MS (n=131), Parkinson's disease (n=47), neuropathy (n=37), post-polio syndrome (n=9), spina bifida (n=23), spinal	HMV	Assessment of data regarding HMV in Ontario (Canada) between 2000 and 2012	HMV incidence, initiation context (in hospital vs home setting), mortality, patient indication	HMV incidence over the 12 year period almost tripled although the reason is not clearly elucidated. Initiation of HMV at home has been well implemented. No change in mortality during the study timeframe. Suggested primary indications are thoracic cage restriction diseases and NMDs. Three main comorbidities were identified: COPD, asthma and congestive heart failure.

Ref. & Type of study	Population & Indication	Therapy	Aim	Evaluation criteria	Results
	muscular atrophy (n=9) and other (n=19)), COPD without other indication (n=878) and unknown indication (n=1690)				
(Tan et al. 2018) A retrospective, single-centre cohort study	240 patients: NMD (n=93), Pulmonary disease (PULM, n=60), non-NMD neuromuscular and chest wall disorders (NMCW, n=51) and OHS (n=36)	HMV	Description of HMV use, survival and predictors of death in Western Australia.	Primary indication for HMV, ventilation interface type (invasive vs noninvasive; mask type; IPAP vs EPAP; mode and backup rate), ventilator adherence, survival status	Only 2 patients were invasively ventilated via tracheostomy, the other patients receive NIV. Survival is strongly linked to the primary indication for HMV. The median survival reported was (95% CI) 1.0 (NMD), 4.2 (PULM), 9.9 (NMCW) and >11.5 (OHS) years. Nevertheless, other factors can influence survival such as age, comorbidities, especially obesity, and FEV_1.
(E. I. Schwarz et al. 2020)	1210 adults with CHRF: NMD or CWD (both groups represent 44%, n=533), COPD (24%, n=296), OHS (17%, n=202), overlap of COPD and OSA (4%, n=52) and others (11%, n=127).	HMV	To examine the long-term clinical outcome data surrounding the death of CHRF patients treated with HMV.	Outcome measures include Kaplan Meier estimates of time-to-death on HMV, ventilation interface type (invasive vs non-invasive), location of death (home vs health centre), cause and assessment of death (respiratory vs non-respiratory and expected vs unexpected), daily usage of HMV, pulmonary functions tests and ABGs when available.	The time-to-death is considerably dependent on the disease group. With the most favourable prognosis on HVM associated to either CWD, myopathy or OHS; contrary to poorer outcome predicted for neuropathies, COPD or traumatic spinal cord injuries. The amount of daily HMV treatment is significantly important in the time-to-death as the patients using NIV for more than 4 hours per day showed longer time-to-death compared to those who use it less ($p<0.001$). No significant difference noted between the other groups. Time-to-death did not depend on type of ventilation interface (invasive vs non-invasive) for all groups.
(Valko et al. 2020) Single centre prospective	66 CRF patients: COPD (n=9), restrictive chest wall disease (n=5), OHS (n=20), non-progressive NMD (n=19) and progressive NMD (n=13)	HMV A40 or Trilogy 100 (Philips)	To evaluate the QoL within the first 6 months after HMV initiation.	HRQL assessment according to the SRI Questionnaire, sleep, anxiety, interface (invasive vs non-invasive) type,	HRQL for patients under HMV seems strongly affected by the initial diagnosis (greatest improvements in QoL observed in COPD and OHS patients versus no change for ALS patients). The type of ventilation interface (invasive vs noninvasive) did not seem to affect HRQL.

Ref. & Type of study	Population & Indication	Therapy	Aim	Evaluation criteria	Results
observational study					
(van den Biggelaar et al. 2020) Randomised trial	95 patients with CHRF, most due to a NMD but a few have a thoracic cage wall disorder.	HMV ResMed ASTRAL 100/150 or ResMed Elisée	Comparing HMV initiation by telemonitoring at home versus in a hospital setting	Primary outcome: $PaCO_2$ Secondary outcome: HRQL (Questionnaires: SRI, MRF-28, SF-36 and HADS) and costs (EQ-5D questionnaire and Dutch reference prices for healthcare consumption, travel and productivity costs).	$PaCO_2$ was significantly increased in both groups ($p<0.01$) but there was no notable difference between groups. Once more, HRQL was significantly improved by HMV set up for both groups but no substantial difference between the two groups was reported. Finally, in the home group a reduction of costs by 3200€/patient was assessed.
(Wilson et al. 2020) SR and MA 33 studies	51085 adult patients with CHRF due to COPD	HMV device or BPAP device	"To evaluate the association of home NIPPV via bilevel positive airway pressure (BPAP) devices and noninvasive HMV devices with clinical outcomes and adverse events in patients with COPD and hypercapnia."	- Primary outcomes: mortality, all-cause hospital admissions, need for intubation, and QoL at the longest follow-up. - Secondary outcomes were hospital admissions for respiratory causes, emergency department visits, ICU admissions, COPD exacerbations, activities of daily living, dyspnoea, sleep quality, exercise tolerance and adverse events.	The use of a noninvasive HMV, when compared with no device, was significantly associated with a lower risk of hospital admission but no significant difference in mortality risk.
(Maquilón et al. 2021) Prospective study	1105 adult patients with CRF on either NIV (n=1047) or IV (n=58). COPD (n=388), OHS (n=264), NMD (n=180), non-cystic fibrosis bronchiectasis or tuberculosis (non-CF BC or TBC, n=92), scoliosis (n=65) ALS (n=58) and other (n=58)	HMV	A prospective examination of patients with CRF admitted to the Chilean national HMV program: data review.	HRQL assessment according to the SRI questionnaire, survival rates (up to 9 years); ventilation interface type (Invasive vs non-invasive)	The most common diagnosis for patients treated with HMV are COPD and OHS with best survival rates reported in OHS, NMD and sclerosis patients. SRI scores showed major improvement over time.

Table 35: Performance of high flow oxygen therapy

Ref. & Type of study	Population & Indication	Therapy	Aim	Evaluation criteria	Results
(Okuda et al. 2014) Case report	1 adult (73-year old) Japanese female with exacerbation of COPD	Nasal high-flow oxygen therapy system: MH-2000 heated humidifier (Pacific-Medico) and a Vivo 30 ventilator (Breas Medical AB),	Case report of sleep-related COPD improved by HFNC therapy.	Apnoea hypopnea index, SpO_2, sleep quality, O_2 narcosis	Increased comfort level for the patient (less claustrophobia) and improved sleep-related alveolar hypoventilation.
(Algamdi et Ball 2016) SR (3RCTs)	Adult patients with AHRF	ns	Determine impact of HFNC therapy on patients with AHRF	Comfort, RR, PaO_2, treatment failure (intubation rate or change to another mode of ventilation), number of ventilator-free days	No conclusive evidence HFNC therapy lowers treatment failure compared to other oxygen therapies. But significantly lower intubations were noted in patients with the most severe forms of AHRF.
(Lara Pisani et al. 2017) Randomised physiologic study	14 patients with COPD	NIV and HHNC (Airvo 2; Fisher & Paykel Healthcare, Auckland, New Zealand)	Comparison of HFNC therapy and NIV on inspiratory effort of COPD patients.	ABGs ($PaCO_2$, PaO_2, PaO_2/FiO_2, $PtcCO_2$), pH, comfort score, TV, inspiratory and expiratory breath durations, patient's own RR,	Both NIV and HFNC therapy significantly improved breathing patterns and reduced inspiratory efforts. But no notable difference in $PaCO_2$ levels, HFNC therapy is a possible treatment for stable hypercapnic COPD patients.
(Vogelsinger et al. 2017) Prospective study	77 CODP patients with stable hypoxemia, already treated with LTOT	Nasal high-flow oxygen therapy system: TNI®20 oxy (TNI medical AG, Würzburg, Germany)	Comparison of HFNC and CO for normo- and hypercapnic COPD patients	ABGs ($PaCO_2$ and PaO_2), SpO_2, FEV1 and oxygen requirement.	Short-term use of HFNC therapy is safe for normo- and hypercapnic COPD patients as it effectively reduces hypercapnia and corrects hypoxemic respiratory failure.
(Longhini et al. 2019)	30 COPD patients with hypercapnic acute	NIV	Assessment of physiological features during	Diaphragm displacement and thickening fraction, ABGs ($PaCO_2$ and PaO_2), pH, RR and comfort.	Improvement of patient comfort and maintenance of diaphragm thickening fraction.

Randomised crossover physiologic study	respiratory failure treated with NIV	Ventilator Servo-I (Maquet Critical Care, Solna, Sweden) and heated humidifier (Optiflow and MR850; Fisher & Paykel Healthcare, Auckland, NZ	HFNC therapy and COT when NIV treatment is discontinued.		
(Lewis et al. 2021) SR (31 RCTs)	5136 patients with respiratory failure admitted to the ICU	HFNC systems: Optiflow, vapotherm,	Comparison HFNC therapy efficacy and safety compared to NIV or NIPPV	ABGs, mortality, length of stay in ICU, RR, Dyspnoea, barotrauma, PaO2/FiO2 ratio, treatment failure rate and comfort scores	HFNC therapy seems to lead to less treatment failure and improvement of the PaO_2/FiO_2 ratio up to 24 hours. But no clear-cut evidence that outcomes measured such as mortality, RR differed between HFNC and standard oxygen therapy.
(Rezaei et al. 2021) Randomised clinical trial	30 adult AECOPD patients	Nasal high-flow oxygen therapy system: TNI medical AG (Würzburg)	To compare HFNC and NIV on AECOPD patients.	ABGs ($PaCO_2$ and PaO_2), pH, RR, dyspnoea score, heart rate, SO_2	HFNC therapy group has significantly higher O_2 saturation levels (p=0.006) and better dyspnoea scores (p=0.02) than NIV group.
(Z. Xu et al. 2021a) MA and SR (25 studies)	2851 patients with COVID-19	Not specified	Assessment of HFNC therapy efficacy in COVID-19 patients.	Intubation, mortality and failure rates, SOFA and APACHE scores, PaO_2/FiO_2, D-dimer, lactate, heart rate, RR, SpO_2/FiO_2, ROX index	HFNC is an effective treatment for patients with COVID-19.

3.10.5 Conclusion

To conclude this part dedicated to the State of the Art, a systematic documentary research was conducted according to a previously defined research plan found in the APPENDIX 4: STATE OF THE ART – LITERATURE SEARCH and the file "**100_66 rev G EO-150_literature_search_protocol"**. This systematic search identified 356 data sets. Following the selection process, 195 data sets were selected and evaluated according to MEDDEV 2.7/1 Rev. Sixteen (16) recommendations and 2 additional data sets were included as manual searches. The list of identified and included/excluded items with reasons for exclusion is detailed in APPENDIX 5: STATE OF THE ART – LITERATUE SELECTION and a separate Literature Research Report file named "**100_66 rev G EO-150_literature_search_report** ". Of the 130 articles included in the State of the Art, 29 were selected to support the performance and safety of HMV, as performance and safety of the home mechanical ventilators could not be separated from the whole system that includes the home mechanical ventilator, tubing, masks or cannulas.
The analysis of those data sets showed that:

- HMV is based on the well-established and documented technology of artificial ventilation by positive pressure dating back to the 1960's.
- HMV can be applied for many indications (COPD, OHS, NMDs…) but more generally for the treatment of patients of all ages with respiratory failure.
- Long term HMV is safe for adults but there is limited data for paediatric patients which needs to be further strengthened.
- Chronic and long-term use of MV is increasingly prescribed thus, HMV is in line with modern medical needs with regards to respiratory failure. Hence, the number of patients prescribed HMV, both short- and long-term is increasing globally. The most common indications for HMV are COPD, OHS, CWDs and NMDs.
- Today MV offers multiple ventilation modes to better suit patient needs.
- HMV initiation seems possible in both a hospital and home setting with no damaging effects on patient outcome and health. In fact, this approach seems beneficial for both the patient, with faster MV implementation, and the healthcare system as it is more cost-effective, frees up hospital resources and medical staff time.
- HMV implementation and telemedicine suggest the need to set up other resources such as on-call medical staff available to assist and intervene upon incident occurrence.
- It has been described that HMV offers benefits such as improved survival, $PtCO_2$, $PaCO_2$ levels, QoL, better overall therapy comfort, improved respiratory compliance and lowers costs, needs for IV as well as exacerbation frequency for COPD patients.
- HFNC therapy is reportedly better tolerated, improves $PaCO_2$ levels and also decreases RR, length of stay in ICU/hospital and exacerbation frequencies (COPD) compared to conventional ventilation therapy. Although often considered louder, overall comfort was deemed better with HFNC therapy.
- The assessments of HRQL have improved but are not consistently carried out.
- High-flow oxygen therapy is increasingly prescribed for severe acute respiratory failure in diseases such as COPD exacerbations and COVID-19 infection.
- In the case of AHRF, prediction of HFNC therapy failure can be strongly correlated to the ROX index and the ratio of oxygen saturation (SpO_2) to RR.
- Further data regarding HMV and HFNC therapy performance is needed as evidence is often considered of low to moderate certainty.
- Reported adverse events are generally linked to the MV itself and not specifically the ventilators. The most common adverse events for HMV are considered non-serious and outweighed by the benefits of MV: discomfort, oro-nasal dryness and skin lesions.
- Reported side effects of HFNC therapy are discomfort linked to heat or thoraco-cervical discomfort as well as varying levels of consciousness
- There is a need for more clear-cut international consensus around HMV practises and patient typology for better stratification.

3.10.6 Degree of novelty

The device does not present innovative features in terms of design, materials, operating principle, technology or medical indications.
The therapy for which the device is used presents well-known risks described in the literature and with similar devices placed on the market with sufficient feedback, i.e.:

- There are therefore **no identified risks** that need to be monitored over the long term and on a larger population.
- There is therefore **no obvious difference** between the duration of pre-market studies and the expected lifetime of the device.

Positive pressure MV is a commonly used solution for the management of respiratory insufficiencies since the 1960's and HMV has been widely developed since the beginning of the 21st century to increase patient comfort but also to help free up overcrowded healthcare establishments. These solutions are associated with few adverse events, most of which are mild and manageable. Based on ANSM criteria (Figure 45), **EO-150 ventilator** corresponds to the following innovation degree: 1 – Lacking or minor novelty (known technology and unchanged clinical impact).

Degré de nouveauté ***Degree of novelty***	**Type de nouveauté** ***Type of novelty***	**Nouveauté à dominante** ***Innovation where the dominant is :***		
		Technologique ***Technological***		**Clinique** ***Clinical***
5	**Innovation majeure** ***Major innovation***	Rupture technologique *Breaking technology*	**et** ***and***	Impact clinique fort *Strong clinical impact*
4	**Innovation** (dispositif innovant) *(innovative device)*	Rupture technologique *Breaking technology*	**ou** ***or***	Impact clinique fort *Strong clinical impact*
3	**Nouveauté substantielle** ***Substantial novelty***	Incrémentation technique *Incremental technology*	**et** ***and***	Impact clinique modéré *Moderate clinical impact*
2	**Nouveauté modérée** ***Modarate novelty***	Incrémentation technique *Incremental technology*	**ou** ***or***	Impact clinique modéré *Moderate clinical impact*
1	**Nouveauté inexistante ou mineure** ***Lacking or minor novelty***	Technologie connue *Known technology*	et	Impact clinique inchangé *Unchanged clinical impact*

Figure 45: Degree of Novelty according to the ANSM criteria

3.10.7 Clinical evaluation strategy

This CER is written in conformity with the demands and requirements of the MEDDEV 2.7-1/Rev 4, MDR 2017/745 and GMED.

According to Section 2 of Chapter I of MDR 2017/745, clinical evaluation is the analysis of "information relating to the safety or performance obtained in the use of a device from the following sources ...":

- the clinical investigation(s) of the device concerned,
- the clinical investigation(s) or other studies cited in scientific publications of a device whose equivalence to the device concerned can be demonstrated,
- reports in peer-reviewed scientific publications on any other clinical experience with the device concerned or with a device whose equivalence to the device concerned can be demonstrated,
- clinically relevant information from post-market surveillance (PMS), in particular post-market clinical monitoring;".

However, Section 61, paragraph 10 of Chapter VI of MDR 2017/745 states: *Without prejudice to paragraph 4, where compliance with the general safety and performance requirements is considered not to have been satisfactorily demonstrated by clinical data, an appropriate justification shall be provided for any such exceptional case based on the results of the manufacturer's risk management and review of detailed data relating to the interaction between the device and the human body, the expected clinical performance and the manufacturer's claims. In this case, the manufacturer shall duly justify in the technical documentation referred to in Annex II why he considers adequate a demonstration of compliance with the general safety and performance requirements based solely on the results of non-clinical test methods, such as technical performance evaluation, bench testing and pre-clinical evaluation.*

This justification enables the writing of a clinical evaluation without clinical performance data.

The manufacturer EOVE claims solely technical performances for the **EO-150 ventilator**. As the **EO-150 ventilator** is not in direct contact with the patient, the benefits to patients and considered indirect. Thus, the direct benefits are attributed to the air or gas/air blend administered to the patient.

In addition, a search of the scientific literature identified performance and clinical safety data on the **EO-150 ventilator** in one data set (Sections 4 and section 5; Appendix 4 and Appendix 5).

Thus, this report focuses primarily on the technical performances of this device as well as its safety during use. The demonstration of device performance and safety is based on:

- A complete State of the Art;
- A description of the risks associated with the use of the medical device;
- Vigilance data, curated data (risk analysis and data from international vigilance databases);
- Compliance to non-clinical elements of common specifications considered relevant to device safety and performance, if applicable;
- Pre-clinical and bench testing / compliance to harmonised standards, if applicable.

Moreover, EOVE commits to perform PMCF monitoring (APPENDIX 3: PMS / CLINICAL / BIOLOGICAL PLAN, "**100_881 rev B : PMCF_plan_EO-150**").

4 SECTION C: REVIEW OF SCIENTIFIC LITERATURE

4.1 CLINICAL DATA FROM THE LITERATURE

4.1.1 Clinical data from the literature for the device under evaluation

Not applicable, see section 3.10.7.
The lack of clinical data on the product was verified through detailed search in the following documents (Appendix 4 and 5):

- "**100_66 rev G : EO-150_literature_search_protocol"**.
- "**100_66 rev G : EO-150_literature_search_report"**.

A literature search on the device under evaluation was nevertheless conducted to determine the availability of technical and safety data. A single data set on the device under evaluation has been identified from the literature search. In this *in-vitro* paper comparing the **EO-150 ventilator** to 7 other home mechanical ventilators, it was shown that this device produces very limited asynchronies as a result of the trigger delay times remaining low (below 200ms) and constant between the different settings. The study found that :

- Ventilators with the highest decrease in tidal volume were the Monnal T50 (64% drop), EOVE (63%), and Weinmann (44%).
- Four of 8 ventilators maintained correct synchronization (cycling in all conditions), despite the changes: EOVE, PB560, Trilogy Evo, and Vivo 60.
- The EOVE, Trilogy Evo, and Astral 150 ventilators delivered VT in all conditions, with little variation, despite decreased effort.
- The lowest trigger delay time variations with changes in mechanics were recorded for the PB560, EOVE, and Vivo 60 ventilators. Ventilatory mode modification from volume control continuous mandatory ventilation (VC-CMV) and pressure support ventilation (PSV) did not cause changes in the trigger response time.
- In VC-CMV the fastest responses (lowest trigger delay times) were achieved by the EOVE and Vivo 60 ventilators.
- The EOVE and Vivo 60 ventilators did not show significant differences with effort decrease or with changes in mechanics, again with trigger delay time values of <200ms.
- The EOVE, PrismaVent, and Astral 150 ventilators registered PTP500 values > 50% of the ideal pressurization with N effort and S mechanics at both levels of PSV, but PTP500 decreased with the L effort.

4.1.2 Clinical data from the literature for the equivalent device

Not applicable. No equivalence is claimed in this CER.

4.2 SUMMARY AND APPRAISAL OF THE CLINICAL DATA

4.2.1 Appraisal of clinical data for the device under evaluation

Not applicable, see section 3.10.7.

4.2.2 Appraisal of clinical data for the equivalent device

Not applicable. No equivalence is claimed in this CER.

4.3 ANALYSIS OF THE CLINICAL DATA

4.3.1 Clinical data on the device under evaluation

Not applicable, see section 3.10.7.

A literature search on the device under evaluation was nevertheless conducted to determine the availability of technical and safety data. A single data set on the device under evaluation has been identified from the literature search. In this *in-vitro* paper comparing the **EO-150 ventilator** to 7 other home mechanical ventilators on an active lung model (ASL 500), it was shown that this device produces very limited asynchronies as a result of the trigger delay times remaining low (below 200ms) and constant between the different settings. The study found that :

- Ventilators with the highest decrease in tidal volume were the Monnal T50 (64% drop), EOVE (63%), and Weinmann (44%).
- Four of 8 ventilators maintained correct synchronization (cycling in all conditions), despite the changes: EOVE, PB560, Trilogy Evo, and Vivo 60.

- The EOVE, Trilogy Evo, and Astral 150 ventilators delivered VT in all conditions, with little variation, despite decreased effort.
- The lowest trigger delay time variations with changes in mechanics were recorded for the PB560, EOVE, and Vivo 60 ventilators. Ventilatory mode modification from volume control continuous mandatory ventilation (VC-CMV) and pressure support ventilation (PSV) did not cause changes in the trigger response time
- In VC-CMV the fastest responses (lowest trigger delay times) were achieved by the EOVE and Vivo 60 ventilators
- The EOVE and Vivo 60 ventilators did not show significant differences with effort decrease or with changes in mechanics, again with trigger delay time values of <200ms.
- The EOVE, PrismaVent, and Astral 150 ventilators registered PTP500 values > 50% of the ideal pressurization with N effort and S mechanics at both levels of PSV, but PTP500 decreased with the L effort.

4.3.2 Clinical data on the equivalent device

Not applicable. No equivalence is claimed in this CER.

4.4 CONCLUSION OF THE LITERATURE REVIEW

Not applicable, see section 3.10.7.

STAGE 1 – IDENTIFICATION OF PERTINENT DATA

5 SECTION D: CLINICAL INVESTIGATIONS AND ASSOCIATED DOCUMENT

5.1 PRE-MARKET CLINICAL INVESTIGATION

Not applicable, see section 3.10.7.

6 SECTION E: POST MARKET SURVEILLANCE (PMS)/PERIODIC SAFETY UPDATE REPORT (PSUR) AND POST MARKET CLINICAL FOLLOW-UP (PMCF)

6.1 POST MARKET SURVEILLANCE (PMS) / PERIODIC SAFETY UPDATE REPORT (PSUR)

Post-market Surveillance of the **EO-150 ventilator** is carried out in accordance with EOVE internal procedure to monitor data on similar devices from the State of the Art and manufacturing incidents that could impact the performance and safety of the device. PMS and vigilance data will be checked every year for the devices that are currently marketed. The PMS data recovered by the manufacturer include the **EO-150 ventilator** and its commercial variants namely, MV-150 and VEMO150.The Periodic Safety Update Report for 2021 is available under the reference "**100_612 E - Rapport annuel de sécurité - PSUR EO-150**".

6.1.1 External complaints

The details of external complaints are described in the file "**100_612 E - Rapport annuel de sécurité - PSUR EO-150**".
Briefly, for the device under evaluation, the **EO-150 ventilator**, the following complaints have been reported:

- in 2021, a serious incident was reported to BfArM involving the sudden stop of ventilation, with audible alarm. Other minor events reported include software bugs and instability of Expired Tidal Volume (ETV)

measurement for very small volumes with false alarm. All the reports were considered without risk to the patients but corrective actions were implemented (AC20-005 and AC21-006).

- In 2020, no serious incidents were identified. The RC20-006 incident reported to BfArM, involving the sudden stop of ventilation without an audible alarm, was not deemed relevant as the **EO-150 ventilator** is not at fault as it was intentionally stopped by a healthcare professional. Four (4) other minor incidents involving software bugs were reported. Risk analysis according to the risk management procedure concluded that the residual risk is acceptable or the level of occurrence is appropriate. Corrective action have been implemented since (AC20-004, AC20-005, AC20-006 and AC20-007).
- In 2019, 3 serious events were reported to BfArM, one was deemed not relevant, the two others were a sudden ventilation shutdown following connection to an external power source (car power source). It was found that previous linking to a damaged EO-BAT9 battery pack was the cause of this issue. The impact on the patient was not specified but corrective action has been taken since (AP19-001). Minor incidents involve premature battery failure (before 2 years) and faulty power supply cards; without risk for the user. Corrective actions have been implemented with regards to minor incidents (AC18-001, AC18-007 and AC19-002).
- In 2018, serious incidents reported to the BfArM include screen/tablet failure and cybersecurity concerns raised by BfArM, battery failure (storage guidelines not followed) and other incident that are not deemed relevant as the ventilator was not at fault. The ANSM reported faulty power cables leading to the shutdown of 3 ventilators: users were warned about the safety risks. Corrective actions have been put in place since such as issuing a field safety notice and reinforcing cybersecurity of the device (AC18-007 and AC18-008). Minor incidents involve premature battery failure (before 2 years) and loss of Bluetooth connection between the ventilation module and the tablet. The implication to the patients' health is not specified but corrective actions were implemented (AC17-012, AC18-001, AC18-006 and AC18-00.
- In 2017, serious events involve the loss of Bluetooth connection between the ventilation module and the tablet. This was considered without risk for the user as the ventilation continued during the error (corrective action : AC17-012). Minor incidents include premature battery failure, software issues and communication issues between the ventilation module and the tablet. Corrective actions were set up to improve Bluetooth connection and FSN were issued (AC17-004 and AC17-012).

Review of the trend report

Analysis of after-sales returns :

Table 36: Returns data for the EO-150 from 2015 to 2020

Year	EO-150 ventilators sold per year	cumulative EO-150 ventilators sold	EO-150 ventilators returned per year	Rate of annual returns / cumulative sales	EO-150 ventilator cumulative returns	Rate of cumulative returns
2015	234	234	14	6%	14	6%
2016	823	1057	115	11%	129	12%
2017	1242	2299	449	19,5%	578	25%
2018	1271	3570	808	22,6%	1386	39%
2019	1036	4606	365	7,9%	1608	35%
2020	1950	6556	339	5,2%	1957	30%

The return rate has continued to fall since the peak of 2018 (annual and cumulative). This is explained by the corrective actions and modifications made since the end of 2018 to make the system more reliable and by the training of customers in maintenance. The cumulative rate of 30% remains above 10% (indicator), but the

increase in the installed base will eventually bring it back to an acceptable threshold (as shown by the annual rate of 5.2%).
In detail, the 365 returns for 2019 were most commonly of the battery, the battery buzzer, the tablet. All 3 represent over half of all returns (64.2%). The following year, 2020 saw 339 returns with the battery tablet, battery buzzer and battery being the 3 most returned units (66.1%).
339 returns for the year 2020, show an evolution for the tablet battery and the new EO-Display.

Table 37: Detail of EO-150 returns in 2019

Battery	Buzzer battery	Tablet battery	CPU card	Turbine	Keyboard	Tablet	EO-Display	Other
146	44	37	25	18	0 - other	44	0 – not sold	51
40.0%	12.1%	10.1%	6.8%	4.9%	0%	12.1%	0%	14.0%

Table 38: Detail of EO-150 returns in 2020

Battery	Buzzer battery	Tablet battery	CPU card	Turbine	Keyboard	Tablet	EO-Display	Other
40	48	136	10	3	8	32	11	51
11.8%	14.2%	40.1%	3.0%	0.9%	2.4%	9.4%	3.2%	15.0%

Before the in-house design of a touch screen (EO-Display), a commercial tablet (ASUS) was used for the user interface. The tablet contains a battery that needs to be replaced after 3 to 4 years of use. This explains the increase of tablet battery returns reported in 2020.
In order to avoid the replacement of this battery and its obsolescence, a hardware and software design modification (MOD20-001) allows the device to operate without regards to the tablet battery. A maintenance kit has been made available since October 2020.
The feedback (11) concerning the new EO-Display actually corresponds to the bugs and screen blockage identified in the customer complaints and corrective actions: AC20-005, AC20-007.

Table 39: Analysis of Non-conformities reported at the final control point during manufacturing

Year	EO-150 ventilators sold per year	Number of design AN/NC-CF*	Rate
2015	234	5	2%
2016	823	13	2%
2017	1242	0	0%
2018	1271	0	0%
2019	1036	2	0.2%
2020	1950	2	0.1%
2021	1230	0	0%

** AN : anomaly ; NC-CF : Non-Conformity - Final Control*

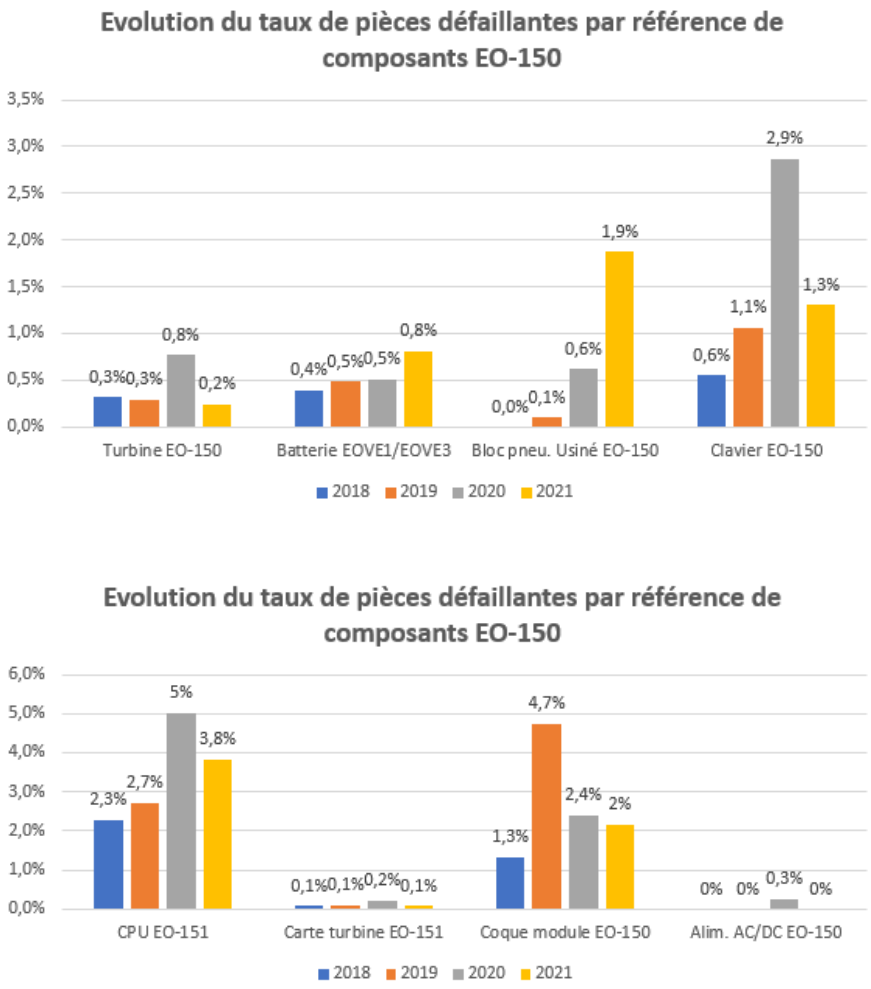


*Figure 46: Evolution of the rate of faulty parts by component reference of the **EO-150 ventilator***

(% of parts qualified as non-conform compared to the total number of delivered ventilators)

The NC parts identified in production and the analysis of their failures or defects show that they are not the cause of customer complaints and incidents. In fact, these NC parts are put aside as they do not pass the checks.

In conclusion, sales estimates reach a total 7778 bases have been sold for 153 incidences reported which represents an incidence frequency of 2 %. Importantly, the frequency of complaints over the years has consistently decreased, meaning that fewer risks remain and corrective actions are efficient, thus, the device is safer.
Complaints filed are mostly about the following issues:

- Software bugs ;
- Instability of expired tidal volume measurement for very small volumes ;
- Battery failure before 2 years (maintenance) with preventive alarm or after prolonged out of specification storage ;
- Batch of faulty power supply cards (overheating of the choke) ;
- Loss of Bluetooth communication between the ventilator module and the station's tablet.

And over half the returns involve the battery, battery buzzer or the tablet battery.

The trends confirm the findings of the materiovigilance and "Customer complaints" chapters. An update of the risk analysis is not required.

6.1.2 Vigilance data

No vigilance data was reported by EOVE concerning the **EO-150 ventilator**.

6.2 POST MARKET CLINICAL FOLLOW-UP (PMCF)

The PMCF plan for the **EO-150 ventilator** is available in APPENDIX 3: PMS / CLINICAL / BIOLOGICAL PLAN and the file "**100_881 rev B : PMCF_plan_EO-150".**

The performance and safety of the **EO-150 ventilator** will be proven from the following sources:

- the clinical investigation(s) of the device concerned ;
- the clinical investigation(s) or other studies cited in scientific publications of a device whose equivalence to the device concerned can be demonstrated ;
- reports in peer-reviewed scientific publications on any other clinical experience with the device concerned or with a device whose equivalence to the device concerned can be demonstrated ;
- clinically relevant information from post-market surveillance (PMS), in particular post-market clinical monitoring.

6.3 DEVICE VIGILANCE THROUGH INTERNATIONAL DATABASES

Verification of international adverse event databases is an important element in the identification of possible risks associated with the medical device. The following adverse event databases were consulted regarding the **EO-150 ventilator** and similar products.

6.3.1 Device under evaluation

The following databases were consulted on the 21st of March, 2022:

- ANSM (France) [http://ansm.sante.fr/Recherche] ;
- TPLC (USA) [https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfTPLC/tplc.cfm];
- Manufacturer and User Facility Device Experience (MAUDE) (USA) [https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/search.cfm] ;
- The Federal Institute for Drugs and Medical Devices (BfArM) (Germany) [http://www.bfarm.de/SiteGlobals/Forms/Suche/EN/];
- Santé Canada (Canada) [https://www.canada.ca/fr/services/sante/securite-produits.html] ;
- Taiwan Food and Drug Administration (TFDA) (Taiwan) [https://www.fda.gov.tw/ENG/];
- Health Regulatory Agency (ANVISA) (Brazil) [https://www.gov.br/anvisa/pt-br/english];
- Ministry Of Food And Drug Safety (MFDS) (South Korea) [https://www.mfds.go.kr/eng/index.do];
- Ministry of Health, Labour and Welfare (MHLW) (Japan) Regulation for Medical Device Recall and Adverse events reporting;
- Medicines and Healthcare products Regulatory Agency (MHRA) (UK) [https://www.gov.uk/drug-device-alerts].

The search terms and the results for each search are presented in the following table and in APPENDIX 6: VIGILANCE DATA FROM INTERNATIONAL DATABASE FOR EOVE, EO-150 AND HOME MECHANICAL VENTILATOR :

*Table 40: Results of the vigilance search for the **EO-150 ventilator** by EOVE*

Database	Search terms	Results
ANSM (France)	EOVE	4 hits, **3** relevant
	EO-150	3 hits, **3** relevant
TPLC (USA)	EOVE	**0** hits
	EO-150	**0** hits
MAUDE (USA)	EOVE	**0** hits
	EO-150	**0** hits
BfArM (Germany)	EOVE	5 hits, **3** relevant
	EO-150	3 hits, **3** relevant
Santé Canada (Canada)	EOVE	**0** hits
	EO-150	**0** hits
TFDA (Taiwan)	EOVE	**0** hits
	EO-150	**0** hits
ANVISA (Brazil)	EOVE	**0** hits
	EO-150	**0** hits
MFDS (South Korea)	EOVE	**0** hits
	EO-150	**0** hits
MHLW (Japan)	EOVE	0 hits, **0** relevant
	EO-150	**0** hits
MHRA (UK)	EOVE	3 hits, **0** relevant
	EO-150	**0** hits

The searches conducted for the **EO-150 ventilator** also include its variants MV-150 and VEMO150.
Of the 18 hits found in the 10 international databases, 12 were relevant.

- ANSM: Both the "EOVE and "EO-150" searches on the ANSM database yielded 3 identical relevant results:
  - 03/09/2018 (n° R1813968): a field service corrective action (FSCA) issued by EOVE for all **EO-150 ventilators** in use to ensure cyber-safety. Although no cyber-attack incident was reported, EOVE identified a potential vulnerability of the wireless functions. A mandatory Software update was carried out and it was recommended to avoid using the smartphone application (VisioControl) until the new software was uploaded.
  - 26/09/2018 (n°R1816630): Field safety notice (FSN) issued by EOVE reminding users that the **EO-150 ventilators'** internal battery is only a backup power source and users need to have an additional power source, such as the EO-BAT9 battery pack. This is especially true for patients with constant MV needs. Moreover, the "DEFAUT CHARGE BAT" and "DEFAUT BAT" alarms verify the performance of the internal battery and this components needs to be swiftly changed in case the alarm is triggered. Finally, back up ventilator should be used, tested and correctly charged every month. No incidents in relation to this issue have been reported.
  - 07/01/2019 (Ref R1813968 – AC18-008 / R1816630 – AC18-007): This FSCA issued by EOVE relates to the FSN issued on 03/09/2018 regarding cybersecurity and the corrective software that has now been made available. This software package consists of three pieces of software, two of which are for the ventilation module referenced C150000500 and P150000400, and one software for the Docking station referenced v7.0.0. And the restrictions regarding the use of the application EO(Remote Vision are lifted as long as the updated versions are used (v7.0.0.). Moreover, for volumetric ventilation modes the insufflation pressure limit can be adjusted to 80 hPa (instead of 60 hPa). This increase in performance is recommended by the ISO 80601-2-72 standard. As a result, the operating time of the **EO-150 ventilator** on its internal battery has been reduced by 20%, to benefit in return of a significant increase of the internal battery life.

This modification is in accordance with our safety information issued the 26th September 2018 (ref R1816630 - AC18-007).

- BfArM: The 3 relevant results found for both searches ("EOVE" and "EO-150") were the same incident reports:
    - 02/11/2017 (ref AC17-012) : Customer safety information issued by EOVE regarding reported incidents of Bluetooth disconnection between the ventilation module and the station without automatic restauration for **EO-150 ventilators** (1% cases). The following mandatory corrective action was implemented: new software download (V5.2.0.).
    - 10/08/2018 (ref AC18-008 - the same ANSM report n°R1813968): FSN issued by EOVE for all **EO-150 ventilators** in use to ensure cyber-safety. Although no cyber-attack incident was reported, EOVE identified a potential vulnerability of the wireless functions. A mandatory Software update was carried out and it was recommended to avoid using the smartphone application until the new software was uploaded.
    - 05/08/2019 (No ref): Supplementary instruction for use issued by EOVE following feedback regarding the use of the **EO-150 Ventilator** connected to the DC power supply system of a car. Additional instructions for the use of the ventilator via a Car lighter DC cable (Ref EO-CARCBL): the engine "Auto START & STOP function" must be deactivated, start the car prior plugging in the Car lighter DC cable, unplug the Car lighter DC cable from the socket in the car prior stopping the engine of the car, do not use the Car lighter DC cable (Ref: EO-CARCBL) if it shows sign of damage or the connector does not show the correct contact arrangement and in case of any doubt about the stability of the DC power supply system of the car or lack of information from the car manufacturer, EOVE recommends to use for ventilator dependent patients the **EO-150 Ventilator** with the EO-BAT9 external battery as external power source.

Some database searches yielded no relevant reports: MHRA (3 hits), TPLC (0 hits), MAUDE (0 hits), Santé Canada (0 hits), TFDA (0 hits), ANVISA (0 hits) and MHLW (0 hits).

All the vigilance data identified (cybersecurity, software bugs, technical issues of sudden Bluetooth connection without automatic reconnection) have been acknowledged and reported by EOVE. The risks have been addressed and handled effectively according to the risk management plan (see file "**100_15 - E - EO 150 Risk management plan**"). No additional risks have been identified.

6.3.2 Similar devices

Next, the same databases were searched for materiovigilance reports regarding similar devices to the **EO-150 ventilator**, as per the search term "home ventilator". The results for each search are presented in the following table and in APPENDIX 6: VIGILANCE DATA FROM INTERNATIONAL DATABASE FOR EOVE, EO-150 AND HOME MECHANICAL VENTILATOR :

Table 41: Results of the vigilance search for home mechanical ventilators

Database	Search terms	Results
ANSM (France)	"Ventilateur à domicile"	31 hits, **9** relevant
TPLC (USA)	"Home ventilator"	2 hits, **2** relevant
MAUDE (USA)	"Home ventilator"	**0** hits
BfArM (Germany)	"Home ventilator"	23 hit, **14** relevant
Santé Canada (Canada)	"Home ventilator"	**0** hits
TFDA (Taiwan)	"Home ventilator"	**0** hits
ANVISA (Brazil)	"Home ventilator"	**0** hits
MFDS (South Korea)	"Home ventilator"	25 hits, **0** relevant
MHLW (Japan)	"Home ventilator"	0 hits, **0** relevant
MHRA (UK)	"Home ventilator"	39 hits, **0** relevant

Of the 120 hits found in the 10 international databases, 25 relevant results were found in the ANSM, TPLC and BfArM databases.

- ANSM, 9 relevant hits:
  - **LUISA ventilator (LM150TD)** from LOWENSTEIN medical (ref R2220972 – 17/08/2022): FSN regarding a potential issue identified by the manufacturer. Rare cases of inspiratory trigger malfunction (firmware version 1.5.0030) may occur when used with a single branch valve circuit. In some cases, the device may trigger additional inspiratory cycles which in turn significantly increases RR causing a risk of ventilation failure. To date, no incidents related to this problem have been reported.
  - **Home ventilators Vivo 45,Vivo 45LS** from Breas (ref R2211302 – 05/05/2022): Corrective measure notice issued by the manufacturer during internal R&D testing. The Vivo 45 and Vivo 45 LS ventilators are equipped with two processors that continuously monitor each other and are programmed to trigger an alarm if it does not receive a signal from the other processor within milliseconds. Internal bench testing found an exceptional condition where the forced shutdown of one of the processors lead to ventilation shutdown without an alarm signal. The probability of harm was estimated to be "Unlikely or less than 2 x 10-8" by BREAS. Corrective action for this issue is the firmware update of Vivo 45 and Vivo45LS ventilators. To date, no incidents related to this problem have been reported.
  - **Trilogy Evo, Trilogy Evo O2, Trilogy EV300** from Philips Respironics (ref n° R2114997 – 10/08/2021): 2 issues have been identified : (1) An increase in expiratory pressure (EPAP/PEP) may occur when the infant/child external flow sensor is used with an active flow circuit or a dual branch flow circuit and manual circuit calibration is performed and (2) pressure variation (by up to 2 cmH2O) during continuous long-term use. Corrective actions for these issues are (1) software update and (2) detailed instructions on how to verify if there have been any significant pressure variations.
  - **Monnal T50** from Air Liquide (ref R2009934 – 15/07/2020) : following multiple field reports, the manufacturer issued a FSN regarding ruptured current interrupt devices (CIDs), that isolate damaged cells of the backup battery. This was found in devices where safety instructions were not followed. Corrective actions were reminded in the FSN : only use the internal battery as a backup power source, the internal battery function must be tested before each use and the use of an external battery pack is mandatory for any portable use of the device.
  - **Trilogy Evo** from Philips (ref R1922023 – 25/11/2019): FSN issued by the manufacturer who identified two unlikely scenarios in which the Trilogy Evo did not immediately and continuously sound the alarm after an untimely processing stop. The cause of this failure to trigger the alarm as intended was the software (versions below 1.02.01.00) not reacting correctly to these events. No corrective actions were suggested. To date, no incidents related to this problem have been reported.
  - **Monnal T40/T50/T60/T75** from Air liquid (ref R1918103 – 29/07/2019) : FSN issued by the manufacturer following a reports involving device contamination. The first issue involves the internal contamination at the inspiratory outlet of the device. These device contaminations occurred in cases where the bacteriological filter was not present on the inspiratory branch. AIR LIQUID reminds the user of the correct instillation, tests, usage and replacement of the bacteriological filters. Second, the reusable silicone membrane of the expiratory valves reportedly harden after multiple cycles of sterilisation (autoclave). Corrective action details new recommended use: this membrane is now single use only.
  - **EO-150 ventilator** from EOVE (ref R1813968, R1816630 and Ref R1813968): all 3 hits are relevant and have been detailed in the previous section (“EOVE” and “EO-150” searches).

- TPLC, 2 relevant hits:
  - “*Continuous, Ventilator, Home Use*”: code NOU/ and regulation number: 868.5895
    Definition: This product c/ode was needed for the home use indication. CBK (“Ventilator, Continuous, Facility Use“) is a device meant for use in medical centres, and NOU is a device intended for home use.

The 3 most common device problems reported were:
  - "Device displays incorrect message", 1025 reports: all reports involve the Astral ventilators (100/150) from Resmed.
  - "failure to calibrate", 995 reports: all reports involve the Astral ventilators (100/150) from Resmed.
  - "battery problem", 340 reports: reports involve the Astral ventilators (100/150) from Resmed or the Vivo40 from Breas.

- "*Ventilator, Continuous, Minimal Ventilatory Support, Home Use"*: code NQY and regulation number: 868.5895
  Definition: This continuous ventilator, which operates using a fixed or passive exhaust port, is intended to treat patients with respiratory failure in the home.
  No adverse events nor complications were reported for this category of devices.

- BfArM, 14 relevant hits:
  - **Carina ™ home** from Dräger medical (ref 00063/09 - 18/12/2008): Important FSN following PMS activities in which the "pilot line disconnect alarm" may not be triggered after pilot line disconnection (an open pilot line may result in a substantial reduction in tidal volume delivery). Appropriate safety measure to apply are detailed in the FSN.
  - **VS III ventilators** from Resmed (ref00403/11 – 09/03/2011): FSN issued by the manufacturer after reports of a software problem with low occurrence (less th/an 1 in 200000 ventilation starts) which /leads to inadequate patient treatment after an unsolicited switch from P1 to P2 ventilation program. This malfunction is thought to have limited health risk in the event it occurs undetected. The corrective action taken by RESMED is a software update (v 1.05).
  - **Trilogy ventilators** from Philips (ref R-09-2011-B – 26/01/2012): FSCA filed by the manufacturer to replace blower motor assemblies. This error could lead to the impeller rubbing against the inner blower motor housing causing noise. To date, there have been no reports of failure, harm or injury due to this condition in the field.
  - **VENTIlogic LS / VENTIlogic plus** from Weinmann (ref 04212/12 - 20/06/2012): important FSN issued by the manufacturer after an error was detected in the device firmware during continuous operation testing. This error could cause the display of the battery charge status to differ from the actual charge status of the internal and/or removable battery. The error can be resolved by an update with new device firmware version (V2.05).
  - **Vivo 50** (ref 07942/14 - 18/11/2014) and **Vivo 60** from Breas (ref 07950/14 - 18/11/2014): two FSCAs issued by Breas who has identified a potential risk associated with its Vivo 50 and 60 ventilators where a keypad malfunction could result in an unintended treatment termination as the device enters stand-by mode with no alarm signals. After enquiries, it was concluded that this type of malfunction is likely to be mostly caused by excessive amounts of cleaning spray/liquid. New firmware has been developed (v2.07 for vivo 50 and v3.05 for vivo 60) to resolve this issue.
  - **Astral** from ResMed (ref 06324/14 - 04/05/2015) + update (ref 09785/15 – 31/12/2015) : FSN issued by the manufacturer following an incident involving circuit disconnection of a patient in a hospital where the device alarms did not operate because all alarms had been disengaged by the physician. Software update will not allow the circuit disconnection alarm for all ventilation modes for dependent patients to be disactivated. And FSN to users will remind them of device use and how to avoid similar issues in future.
  - **Vivo 60** from Breas (ref 08689/15 - 11/11/2015): The manufacturer has identified necessary improvements for the Vivo 60 ventilator (and paediatric dual limb inserts, ref 005525). Indeed, certain delivered Paediatric Dual Limb Inserts may not fully meet their specifications in terms of Vte/Mme measurements and leaks. Breas has updated and improved their product verification process of these pieces and replacement parts will be provided. No incidents and very few complaints related to this have been reported for the Vivo 60 ventilator.

- **Astral 100/150** from Resmed (ref 06789/16 – 12/08/2016): FSN issued by the manufacturer following field incidents of internal electrical issues that led to ventilator shutdown without a low battery alarm of the critically low battery alarm activation (the same lack of alarm triggering was also reported for the Astral external battery). Corrective action taken by the manufacturer is the change of devices' design to address the cause of the issue. Faulty devices are replaced.
- **CARAT I pro and CARAT II Pro** ventilators from Hoffrichter (ref 08594/16 – 21/12/2016): important FSN issued by the manufacturer regarding a FSCA to resolve a software bug in which the user could start the ventilator with the factory settings. These settings are not adapted to efficiently and safely treat patients. No reports of patients being harmed by this issue has been identified so far.
- **Vivo 60** from Breas (ref 10621/17 - 19/10/2017): Urgent FSN issued by the manufacturer who has identified a potential risk associated with its Vivo 60 ventilators in configurations with a dual- or single-limb circuit with exhalation valve. Due to an error in the moulding process of the Outlet Cover in one batch, there may be a risk that the hole in the centre of the outlet tube (controlling the exhalation valve) may be partially or completely obstructed by residual plastic material. BREAS initiates a mandatory replacement of the Outlet Covers in all devices that have been identified as potentially involved.
- **Stellar 100/150** from Resmed (ref 16566/19 – 16/12/2019): Urgent FSN issued by the manufacturer following an incident in which the alarm buzzer did not function as a result of software and component failure. RESMED recommends carrying out alarm tests when using the device.
- **Vivo 55/65** from Breas (ref 01793/20 - 06/02/2020): Urgent FSN issued by the manufacturer after an incident was reported involving a Vivo 55 protective cover. The interior of the Protective Cover may, under certain circumstances i.e. if significant force is applied to the Protective Cover, obstruct the outlet orifice for the exhalation valve control pressure. This may cause exhaled air to remain in the patient circuit and the ventilator will consequently alarm for Rebreathing and subsequently an Exhalation Valve Failure alarm with high priority audible and visual signals after approximately 60 seconds. Correction actions include replacing a protective cover if needed and inform the user of new precautions when using the cover.

For some databases no relevant reports were identified: MAUDE (0 hits), Santé Canada (0 hits), TFDA (0 hits), ANVISA (0 hits), MFDS (25 hits) MHLW (0 hits) and MHRA (39 hits). Irrelevant results were either about non-home mechanical ventilators or unrelated topics.

All the vigilance data identified (firmware/software bugs, stability and internal battery issues) have either been acknowledged and reported by EOVE or are specific to the device/manufacturer and thus, are not transposable to the **EO-150 ventilator**. The risks have been addressed and handled effectively according to the risk management plan (see file "**100_15 - E - EO 150 Risk management plan**"). No additional risks have been identified.

6.4 USABILITY

The usability of the **EO-150 ventilator** was assessed by studies following the method and criteria defined in the usability formative validation plan "**100_341 D - Usability formative validation plan**".
The formative test for the usability of the **EO-150 ventilator** took place between the 30th of June 2021 and the 5th of July 2021 with EOVE employees. It was tested using the formative evaluation form with the user identified in the protocol (see "**100_342 D - Usability formative validation report**" word and excel files and "**100_349-B - Usabililty summative validation_report**").
The completed evaluation forms are available in the file "**100_348 B- Usability summative validation plan** " and the results are summarized in the next table:

N° of function	Main function of service	Users	Usability specification	Acceptance criteria (protocol)	Results
Transport					
1	Use of transport bag	family, technician	Installation in the transport bag must be completed in less than 5 minutes.	60% of tester successful in less than 5 minutes.	All testers were successful PASS
2	Installation of the travel bag on a wheelchair	technician	The installation of the travel bag on the wheelchair (or equivalent) must be carried out in less than 5 minutes.	60% of tester successful in less than 5 minutes.	All testers were successful PASS
3	Installation of the cigarette lighter cord	family	The installation of the cord and storage in the travel bag must be done in less than 2 minutes.	60% of tester successful in less than 2 minutes.	All testers were successful PASS
4	Installation on the trolley	clinician, technician	Installation of the ventilator on the trolley should be completed in less than two minutes.	60% of tester successful in less than 2 minutes.	All testers were successful PASS
5	Installation with upright brakets	family, clinician	Installation of the ventilator on the upright brackets is done in less than 5 minutes, without fall of the device.	60% of tester successful in less than 2 minutes.	83% of the testers were successful PASS
Installation					
10	Ventilator installation	family, clinician	The installation of the ventilator (out of the bag with its accessories) must be carried out at the patient's bedside in less than 2 minutes.	60% of tester successful in less than 2 minutes.	All testers were successful PASS
11	Mains connection	family, clinician	The connection to the mains must be made in less than 1 minute.	100% of tester successful in less than 1 minute.	All testers were successful PASS
13	Power supply signaling	family, clinician	It is visible at 1m	100% of tester successful	All testers were successful PASS
14	Battery level signaling	family, clinician	It is visible at 1m	100% of tester successful	All testers were successful PASS

N° of function	Main function of service	Users	Usability specification	Acceptance criteria (protocol)	Results
15	Battery charging signaling	family, clinician	It is visible at 1m	100% of tester successful	All testers were successful PASS
16	Installation of the patient circuit	family, clinician, technician	The installation of the pipes must be carried out in less than 5 minutes in the different configurations (single branch, double branch and leakage circuit)	60% of tester successful in less than 5 minutes.	All testers were successful PASS
17	Insertion of the module into the station	family	Module insertion must be completed in less than 30 seconds	100% of tester successful in less than 30s.	All testers were successful PASS
18	Extracting the module from the station	family	Module extraction must be completed in less than 30 seconds	100% of tester successful in less than 30s.	All testers were successful PASS
Ventilator functions					
30	Starting ventilation	family, clinician	The ventilation must be started in less than 10 seconds.	100% of tester successful in less than 10s.	All testers were successful PASS
31	Stopping ventilation	family, clinician	The ventilation must be stopped in less than 30 seconds.	60% of tester successful in less than 30s.	All testers were successful PASS
32	Warning audible alarms	family, clinician	It is audible at 1m	100% of tester successful	All testers were successful PASS
33	Visual alarms warning	family, clinician	It is visible at 1m	100% of tester successful	All testers were successful PASS
34	Silence the alarm	family, clinician	Alarm inhibition / cancellation must be completed within 30 seconds.	60% of tester successful in less than 30s.	All testers were successful PASS

N° of function	Main function of service	Users	Usability specification	Acceptance criteria (protocol)	Results
35	Ventilator start-up	family, clinician	Ventilator start-up should be completed within 10 seconds.	100% of tester successful in less than 10s.	All testers were successful PASS
36	Ventilator stop	family, clinician	The ventilator must be switched off within 30 seconds.	60% of tester successful in less than 30s.	83% of the testers were successful PASS
37	eo-display start-up	technician	Eo-display start-up should be done in less than 1 minute.	60% of tester successful in less than 1 minute.	All testers were successful PASS
38	eo-display stop	technician	Eo-display stop should be done in less than 1 minute.	60% of tester successful in less than 1 minute.	All testers were successful PASS
39	Presets selection	family, clinician	The present application must be done in less than 10 minutes	60% of tester successful in less than 10 minutes.	All testers were successful PASS
40	Unlocking setting screen	clinician, technician	Unlocking the main menu must be done in less than 5 minutes.	60% of tester successful in less than 5 minutes.	All testers were successful PASS
41	Circuit patient calibration	Patient/family, clinician, technician	Calibration circuit must be done in less than 5 minutes.	60% of tester successful in less than 5 minutes.	All testers were successful PASS
42	Patient type setting	clinician, technician	Patient type setting must be done in less than 5 minutes.	60% of tester successful in less than 5 minutes.	All testers were successful PASS
43	Circuit type setting	clinician, technician	Circuit type setting must be done in less than 5 minutes.	60% of tester successful in less than 5 minutes.	All testers were successful PASS

N° of function	Main function of service	Users	Usability specification	Acceptance criteria (protocol)	Results
44	Ventilation mode selection	clinician, technician	Ventilation mode selection must be done in less than 5 minutes.	60% of tester successful in less than 5 minutes.	All testers were successful PASS
45	Adjustment of ventilation settings	clinician, technician	Adjustment of ventilation settings must be done in less than 5 minutes.	60% of tester successful in less than 5 minutes.	All testers were successful PASS
46	Visualization of measurements	clinician, technician	The access to monitoring screen must be done in less than 5 minutes.	60% of tester successful in less than 5 minutes.	All testers were successful PASS
47	Plugin and unplugging of the remote alarm	technician	The installation of the remote alarm is done in less than 2 minutes The deinstallation of the remote alarm is done in less than 1 minutes	60% of tester successful in less than 2 and 1 minutes	All testers were successful PASS
Maintenance					
60	Air inlet filter replacement	technician	Replacing the air inlet filter should be done in less than 5 minutes.	60% of tester successful in less than 5 minutes.	All testers were successful PASS
61	Internal battery replacement	technician	Replacing the internal battery should be completed within 10 minutes.	60% of tester successful in less than 10 minutes.	All testers were successful PASS
65	Double branch replacement	technician	The replacement of the double limb should be carried out in less than 5 minutes.	60% of tester successful in less than 5 minutes.	All testers were successful PASS
66	Cap + membrane replacement	technician	The replacement of the cap and the membrane should be done in less than 5 minutes.	60% of tester successful in less than 5 minutes.	All testers were successful PASS
67	Retrieve of data from the device through USB (Eo-display station)	technician	Generation must be started in less than 5 minutes. Retrieval must be started in less than 1 minute.	60% of tester successful in less than 6 minutes	All testers were successful PASS

N° of function	Main function of service	Users	Usability specification	Acceptance criteria (protocol)	Results
68	Recycling of the ventilator and circuit components	technician	The process in place for the recycling of the ventilator and circuit components can be taken into account and applied.	NA for formative evaluation	

Non user errors or hazards had been discovered during the usability tests. The usability tests performed on the last version of the interface permit to validate the expected usability of the interface.

6.5 CONCLUSION

In conclusion, the 37 relevant complaints filed and international vigilance data regarding the **EO-150 ventilator**, or similar devices, are comparable and are as follows:

- Cyber security measures (**EO-150 ventilator**);
- Internal battery preventative safety measures (**EO-150 ventilator**);
- Insufflation pressure limit adjusted for volumetric modes (**EO-150 ventilator**);
- Wireless connection loss without automatic restauration (**EO-150 ventilator**);
- Issues with car DC power supply (**EO-150 ventilator**);
- Software/firmware issues (alarm triggers, keyboard, wrong settings, battery life indicator wrong,…) (**EO-150 ventilator** and similar devices);
- Processor malfunction (similar devices);
- Battery CID rupture (similar devices);
- Device contamination (similar devices);
- Expiratory valve damage (similar devices);
- Failure to calibrate (similar devices);
- Manufacturing errors (moulding, assembly) (similar devices).

Moreover, the usability formative tests of the latest version of the **EO-150 ventilator** showed minor errors that were made by various types of users. But all tests were passed thus, the usability of the device as well as the information provided by the manufacturer allow for correct use of the device.

These incidents can be hazardous to patient health but all the issues mentioned are well-known and corrective actions were always put in place by EOVE to resolve or limit them.

7 SECTION F: INSTRUCTIONS FOR USE, SUMMARY OF SAFETY CHARACTERISTICS AND CLINICAL PERFORMANCE, LABELS AND OTHER INFORMATION SUPPLIED WITH THE DEVICE

This CER covers the **EO-150 ventilator** and its commercial variants namely, MV-150 and VEMO150. Hence, in this next section, the term "**EO-150 ventilator**" also refers to the two variants.

7.1 HAZARDS ANALYSIS FROM RISK MANAGEMENT DOCUMENTS

7.1.1 Initial risk management

A risk analysis of the **EO-150 ventilator**, compliant with the following standards, was conducted:

- ISO 14971: Medical devices – Application of risk management to medical devices.
- IEC 60601-1: Medical electrical equipment – Part 1: General requirements for basic safety and essential performances.

- IEC 60601-1-2: Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performances - Collateral standard: Electromagnetic compatibility - Requirements and tests.
- IEC 62304: Medical device software - Software life-cycle processes.
- ISO 80601-2-72 Medical electrical equipment — Part 2-72: Particular requirements for basic safety and essential performance of home healthcare environment ventilators
- EU 2017 / 745 medical device regulation
- Directive 93/42 CEE (until the transition to the EU 2017/745 regulation)
- DORS/98-282: Règlement sur les instruments médicaux (RIM)
- RESOLUTION – RDC No. 16 March 28, 2013 – Brazilian regulation

The risk management process of this project is conform to the procedure PR04: "**PR04 – J - Risk management**", to the risk management plan and the cybersecurity risk management plan. See document "**100_67 - rev I - Risk management report"**.

It must be noted that the additional risk analysis file, **"100_813 rev B Cybersecurity Risk Analysis",** completes the **EO-150 ventilator** Risk analysis by adding the risks specific to cybersecurity. It applies to the **EO-150 ventilator** with its ability to be connected to the Vestalis web platform with a USB 4g dongle.

The aim of the risk management is to identify the hazards associated to the product, evaluate the associated risks and manage these risks. This review is done at least every year.

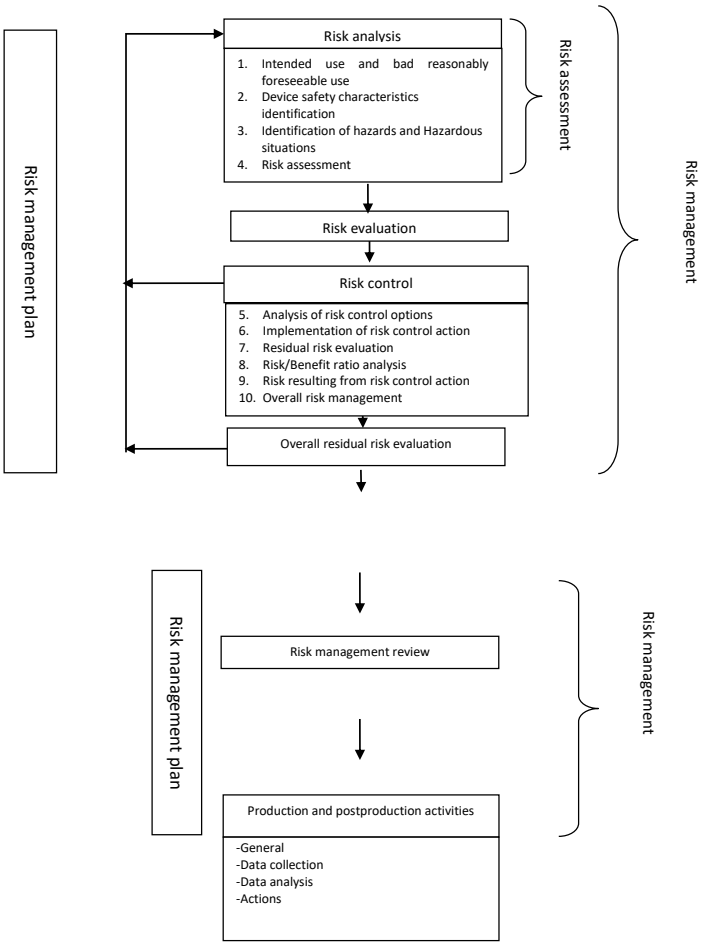


Figure 10: Requirements and steps for risk analysis

The identification of dangerous situations in a systematic and objective way is achieved by taking into account the IEC 60601-1 hazards and another specific norms of medical devices, the dangerous situations identified, which can be also requested by the essential requirements of Directive 93/42/EEC or 2017/745 medical device regulation ; the warnings, and recalls come from health authorities for the equivalent medical devices in the field. The risks are then evaluated based on the Severity of damage, probability of the Occurrence of damage, Detectability of the damage according to the criteria defined below.
For each identified hazard, a probability of occurrence and a degree of gravity for the patient is determined, as described in the following table:

Table 42: Severity, probability of occurrence of a hazard and detectability of risks for the EO-150 ventilator during the design phase

Severity	
Catastrophic: 10	Catastrophic injuries or serious damage that can result in death. Critical injuries or irreversible damage, totally inadequate treatment, permanent disability.
Significant: 7	Lesions or reversible damage requiring medical treatment, temporary disability
Minor: 3	Minor injuries or damage reversible without medical procedure
Negligible: 1	Slight discomfort or inconvenience

Probability of occurrence	
Frequent: 10	Occurs almost every time in the lifespan of the device or patient treatment (days).
Probable: 7	Likely to occur often in the lifespan of the device or patient treatment (months).
Sure: 3	May occur occasionally at least once in the lifespan of the device or patient (years).
Systemic: 1	May occur rarely under special conditions at least once in the lifespan of the N device or N patients treatment.

Detectability	
Impossible: 10	The damage cannot be prevented.
Possible: 7	During maintenance, final control of the device (every year). The health personals, family assist the patient during the therapy and the patient distress or injury can alert, but with reversible damage.
Sure: 3	Cautions, safety controls before start and stop the device every day The health personals, family assist the patient during the therapy and the patient distress or injury is evident to see without damage.
Systemic: 1	An alarm prevents the user every time

The risk level is given by combining the three parameters: **Severity x Probability x Detect ability**.

The risk acceptance is given by the following rule:
Intolerable risk: if the risk level is equal or higher than 300. This final level is identified by a red colour in the risk analysis.

Risk as low as is reasonably possible (*aussi faible que raisonnablement possible* : AFQRP): Acceptable Risk with specified conditions: if the risk level is lower than 300 and greater than or equal to 101. This final level is identified by an orange colour in the risk analysis.

Unconditional acceptable risk: if the risk level is equal to or lower than 100. This final level is identified by a green colour in the risk analysis.

Risk management

The risk analysis of the product may be updated following a corrective action plan, a request of design modification, a vigilance issue, a customer complaint or minor design improvement. For these situations, the Risk Management Report is updated periodically in a way to match with the current version of Risk Analysis of the

product, and especially when the Risk Analysis modification impacts the conclusion of the Risk Management Report, the acceptable residual risks and the global residual risk.

Assessment of the acceptability of the residual risks: after the implementation and verification of all measures to control risks, residual risks presented by the medical device, taken together, are reviewed to determine whether they are acceptable.
The risk management plan defines the criteria to evaluate and accept the residual risks. The acceptable residual risk can result in modifications to the information provided to the user or patient (user manual).

An "Excel" table is annexed to this document and it records the risk analysis of the **EO-150 ventilator** ("**100_17 AI Risk analysis"** and **"100_813 rev B Cybersecurity Risk Analysis"**), with applicable chapters of the ISO 14971 norm:

- Risk evaluation for each dangerous situation (§4),
- Risk evaluation (§5),
- Risk control (§6).

In total, **550** risks related to the device were identified via risk analysis. Of these, risks were grouped into categorises as follows:

- Attacker (cybersecurity issues) : 20 risks were identified;
- Design : 258 risks were identified;
- Design + user: 29 risks were identified;
- User: 195 risks were identified;
- Remote Android: 1 risk was identified;
- Environment: 1 risk was identified.

The Residual Risks (RR) identified in the document "**100_17 Rev AI Risk analysis"** are the following:

- Rr1: Installation not conform / drop of ventilator
- Rr2: Bag installation not conform / drop of ventilator

Acceptance criteria of residual risks:
To be accepted, a residual risk must answer criteria 1 or 2 (or both) below:
Criteria 1: Risk perfectly known and identified by the norms of safety or collateral norms applied to the device; and mandatory explicit mention in the user manual with an "ATTENTION" or "WARNING" note.
Criteria 2: Risk known inherent to the similar devices available on the market (see State of the Art).

Otherwise the benefit / risk should be argued for accepting the residual risk.

Table 43: Residual risk acceptance criteria

N°	Dangerous situation & default	Crit. 1	Crit. 2	Explanation	RR accepted Yes/No
Rr1	Installation not conform / drop of ventilator	yes	yes	1/ Risk identified in the norm IEC 60601-1 and IEC 60601-1-11, with warning in the user manual. i.e. M36: warning: drop of ventilator - user manual. 2/ The ventilator moves and could not be screw with tool (wall, table)	Yes
Rr2	bag installation not conform / drop of ventilator	no	yes	2/ The home care ventilator is movable per definition and follows the patient daily. The utilisation of the transport bag is described in the user manual with the warnings. i.e. M120: warning ; bag installation against drop - user manual	Yes

The Residual risks identified for the **Unconditional acceptable risks**

Recall: The residual risk is accepted without condition because the risk level is acceptable (equal or lower than 100). But it mandatory addresses an ATTENTION or WARNING in the user manual.

The generic Residual Risks (RRxg) identified in the document "**100_17 AI Risk analysis**" are the following :

rr1g: Desaturation of disabled patient without surveillance
rr2g: hypercapnia for disabled patient without surveillance
rr3g: barotrauma for disabled patient without surveillance
rr4g: Desaturation of the patient under physician care
rr5g: Burn of the user or of the patient
rr6g: Desaturation of the patient after wrong maintenance operations
rr7g: Drowning of disabled patient without surveillance
rr8g: Cardiac dysfunctions for disabled patient without surveillance

The Residual Risks rr1g, rr2g, rr3g, rr4g, rr7g, rr8g are addressed by the WARNING: " A ventilator dependent patient should always be monitored by trained personnel ".

The Residual Risk rr5g is addressed by the WARNINGS:
'The oxygen flow must be turned off when the device is not ventilating so that oxygen does not accumulate within the device. The accumulation of oxygen presents a fire risk'.
'Oxygen supports combustion. Only use oxygen in well-ventilated rooms. Using oxygen while smoking or in the presence of an open flame creates a fire hazard'.
'Replacement of lithium batteries or fuel cells by anyone other than trained personnel will result in dangerous risk (e.g., excessive temperatures, fire or explosion)'.

The Residual Risk rr6g is addressed by the WARNING: 'Maintenance of the ventilator should be carried out by a trained technician. Attempting to repair the machine yourself could result in patient injury or damage to the machine'.

No residual risks were left unaccepted in the cybersecurity risk file and no new risks emerged as a result of risk mitigation.

Acceptance criteria of the global residual risk:

100 % of the residual risks are accepted.
This takes into account all residual risks, assures the benefits of the intended use of the medical device, and that the medical device is safe. cf. §8.1 - ISO-TR-24971-2020.

Overall, the residual risks have been reduced: 8 acceptable residual risks remain. These risks are acceptable because they have been reduced to as low a level as possible and because a relative warning now features in the user manual.

The benefit-risk balance is entirely in favour of the benefit of treating these patients; the absence of ventilation treatment (when indicated) is a considerable loss of opportunity, reducing QoL and increasing hospital use, and for the most severe patients reducing survival.

7.1.2 Global conclusion on risk management

The **"100_67 - rev I - Risk management report"** document confirms the complete review of risk management activities, of their implementations, the acceptation of the residual risks and global residual risk, and that appropriate measures are taken for the survey activities of production and postproduction.

7.2 INFORMATION PROVIDED BY THE MANUFACTURER

Information materials are supplied by the manufacturer together with the **EO-150 ventilator**, in order to ensure appropriate handling and use of the device.
The document references are listed in the table hereafter.

Table 44: Information provided by the manufacturer

Document	References
Website	EOVE website/EO-150 ventilator and accessories
Catalogue	**"Catalogue EOVE Rev3_7 juin 2021 (1)"**
Instructions for Use	**"100_23 : user manual_EO-150_ revDE"**
Label	**"100_23 : user manual_EO-150_ revDE"**

STAGE 2 – APPRAISAL OF PERTINENT DATA

Not applicable, see section 3.10.7
The performance and safety of the **EO-150 ventilator** will be proven by an evaluation of:

- Complete State of the Art;
- A description of the risks associated with the use of the medical device;
- Complications associated with the devices;
- Complaints, vigilance and materiovigilance curated data;
- Compliance to non-clinical elements of common specifications considered relevant to device safety and performance, if applicable:
- Pre-clinical and bench testing / compliance to standards, if applicable.

Moreover, EOVE commits to perform PMCF monitoring in order to obtain data concerning the three devices evaluated (APPENDIX 3: PMS / CLINICAL / BIOLOGICAL PLAN, "**100_881 rev B : PMCF_plan_EO-150**).

STAGE 3 – ANALYSIS OF CLINICAL DATA

Not applicable, see section 3.10.7
The performance and safety of the **EO-150 ventilator** will be proven by an evaluation of:

- Complete State of the Art;
- A description of the risks associated with the use of the medical device;
- Complications associated with the devices;
- Complaints, vigilance and materiovigilance curated data;
- Compliance to non-clinical elements of common specifications considered relevant to device safety and performance, if applicable:
- Pre-clinical and bench testing / compliance to standards, if applicable.

Moreover, EOVE commits to perform PMCF monitoring in order to obtain data concerning the three devices evaluated (APPENDIX 3: PMS / CLINICAL / BIOLOGICAL PLAN, "**100_881 rev B : PMCF_plan_EO-150**).

8 SECTION G: SUMMARIES OF ALL AVAILABLE DATA AND CONCLUSION

This CER covers the **EO-150 ventilator** and its commercial variants namely, MV-150 and VEMO150. Hence, in this next section, the term "**EO-150 ventilator**" also refers to the two variants.

8.1 SUMMARY OF CONFORMITY ASSESSMENT OF SAFETY (GSPR 1 and GSPR 4)

The safety of the **EO-150 ventilator** is proven through :

- an evaluation of a complete State of the Art;
- the evaluation of clinical data from similar therapies;
- risk management output (a description of the risks associated with the use of the medical device);
- compliance to non-clinical elements of common specifications considered relevant to device safety and performance (if applicable);
- complaints/vigilance data of the **EO-150 ventilator** and similar medical devices;
- pre-clinical data.

The clinical safety claims for the medical device **EO-150 ventilator** are:

- safe for adults and children (over 3.5kg);
- suitable for use in hospitals, medical centres or at home;
- deployment of a backup ventilation module in case of failure.

8.1.1 State of the Art

The literature underlines the safety of HMV in the context of artificial ventilation, which is generally carried out in hospitals and healthcare centres so far. Findings demonstrate that HMV initiation and long term treatment are possible in a home setting with no damaging effects on patient outcome and health (COPD Working Group 2012; Duiverman et al. 2020; HAS, COPD care guideline 2019; Kopsaftis et al. 2020; P. B. Murphy et Hart 2014; P. B. Murphy, Arbane, Phillips, et al. 2017; P. B. Murphy, Arbane, Bisquera, et al. 2017; Pallero et al. 2014; Suh, Murphy, et Hart 2019a; Wilson et al. 2020).
Moreover, two studies have specifically assessed the performance and safety of HMV in children as young as 28 days of age (Racca et al. 2011; Mandelzweig et al. 2018), and although the data is very promising it is still lacking and should be further strengthened.
Furthermore, reported adverse events are generally linked to the MV itself and not specifically the ventilators. Adverse events for HMV are well known, manageable and largely outweighed by the benefits. The most commonly reported side effects are discomfort, oro-nasal dryness, skin lesions, dyspnoea and claustrophobia (see section 1.13.4.9. for the full list).

8.1.2 Risks analysis

A risk analysis of the **EO-150 ventilator**, following the requirements of the standard ISO 14971:2019 + A11 2021 *Medical Devices—application of Risk Management to Medical Devices*, is available in the risk management report: "**100_67 - rev I - Risk management report"** (see section 7.1).

The aim of the risk management is to identify the hazards associated to the product, evaluate these risks and manage them. In total, **550** initial risks were identified for the **EO-150 ventilator.** All risks were managed by EOVE to control and mitigate them. The risks related to usability identified in the risk analysis was deemed to be acceptable. Thus, proving that this device is appropriate for use by the intended population in a home setting. Additionally, the EOVE team identified cybersecurity risks and that were analysed and mitigated before incidence occurrence. The risk analysis performed for the **EO-150 ventilator** showed that, after risk management, **8** residual risks remained. All were deemed acceptable after a warning in the user manual was added. These risks and their mitigations are detailed in the updated risk analysis file "**100_017 rev AI Risk analysis"** and new "**100_813 rev B Cybersecurity Risk Analysis** ".

Overall, the residual risks have been reduced to as low a level as possible: 100 % of residual risks are accepted (**8**) and the global residual risk is acceptable. The updated risk analysis "**100_017 rev AI Risk analysis "** and "**100_813 rev B Cybersecurity Risk Analysis**" cybersecurity risk analysis did not identify any new residual risks. And thus, did not change the acceptability of the global residual risk.

The short- and medium-term safety of the **EO-150 ventilator** is validated based on the mitigation measures put in place by EOVE, as well as the absence of emergent risks and new safety concerns.

8.1.3 PMCF

No pre-market clinical investigation and PMCF have been done on the **EO-150 ventilator** as only technical performances are claimed. A plan describing the future PMCF activities on the **EO-150 ventilator** is available in the document "**100_881 rev B : PMCF_plan_EO-150**" to gather satisfactory data regarding the performance and safety of the **EO-150 ventilator**.

8.1.4 PMS/PSUR

To identify possible risks associated with the medical device, the PMS/PSUR plan includes a verification of international adverse events databases. In total 138 events were found of which 37 were considered pertinent to the **E0-150 ventilator** device (see section 6.3). Reports include issues with cybersecurity, software/firmware bugs, internal battery damage, etc. Of these identified events, all are already known to the manufacturer and included in the manufacturer's risk analysis.

Moreover, PMS for the **E0-150 ventilator** have shown that between 2017 and 2021, 153 incidents have been reported for 7786 units sold. This translates into an incidence frequency of 2%. In addition, the suitability for use of the **EO-150 ventilator** was assessed by reviewing the complaints received by EOVE including the vigilance data regarding this device. All of the complaints were delt with and reported incidents are in line with the international materiovigilance data. The safety claims regarding the implementing of alarms to safeguard against unexpected device shutdown are backed up by vigilance data. Indeed, an incident reported could have been avoided if the alarm had not been disabled by the user *(***Astral** from ResMed (ref 06324/14 - 04/05/2015) + update (ref 09785/15 – 31/12/2015)*).* Thus, this demonstrates the importance and efficacy of the alarms installed in the **E0-150 ventilator** to ensure its safety.

Additionally, all the complaints involve risks that have been included and assessed in the risk analysis and management documents (see section 7.1).

The essential safety requirements of the device are met in accordance with the analysis of incidents & complaints from the field and the risk management report conclusions.

8.1.5 Contraindications/Complications

The following contraindications are identified by EOVE for the **EO-150 ventilator**:

Contraindications according the user manual

- Severe hypotension especially with decreased intravascular volume;
- Pneumothorax/pneumomediastinum;
- Brain surgery or head trauma;
- Cerebrospinal fluid leakage;
- Dehydration;
- Bullous emphysema.

According to the literature, other than patient refusal or physical obstruction, there are no clear-cut contraindications for MV (Wolfram Windisch et al. 2018).

The following adverse effects are identified by EOVE for the **EO-150 ventilator**:

Adverse Effects according the user manual

- Dry mouth/nose;
- Eye irritation;
- Bloating;
- Gastric distension;
- Skin wound;
- Sinus discomfort;
- Aerophagia;
- Claustrophobia;
- Excessive dyspnoea/ventilation dyspnoea;
- Lung injury (including barotrauma and volotrauma);
- Increased secretions;
- Heat discomfort (only for c-flow mode);
- Thoracic discomfort (only for c-flow mode).

All of the following adverse events reported in the literature have been identified and addressed by the manufacturer:

- Classical MV modes
  - Abdominal distension (Pallero et al. 2014)
  - Aerophagia (Duiverman et al. 2020)
  - Barotrauma (Lewis et al. 2021)
  - Claustrophobia (Afshar et al. 2020; Pallero et al. 2014; Sinuff, Keenan, et Department of Medicine, McMaster University 2004)
  - Discomfort (Duiverman et al. 2017; Ergan et al. 2019; Kopsaftis et al. 2020; L. Pisani et al. 2019; Sinuff, Keenan, et Department of Medicine, McMaster University 2004; Z. Xu et al. 2021b)
  - Dyspnoea (Lewis et al. 2021; Stieglitz et al. 2013; 2017)
  - Excessive 'deventilation dyspnoea' (Duiverman et al. 2020)
  - Eye irritation (Afshar et al. 2020; Nishimura 2016)
  - Gastric distention (Afshar et al. 2020)
  - Increase of secretion (Stieglitz et al. 2017)
  - Oro-nasal dryness (Afshar et al. 2020; Duiverman et al. 2020; Kopsaftis et al. 2020; Lewis et al. 2021; Nishimura 2016; L. Pisani et al. 2019)
  - Rhinitis (Afshar et al. 2020; Pallero et al. 2014)
  - Skin lesion (Afshar et al. 2020; Ergan et al. 2019; Lewis et al. 2021; Mandelzweig et al. 2018; Pallero et al. 2014; L. Pisani et al. 2019; Sinuff, Keenan, et Department of Medicine, McMaster University 2004; Z. Xu et al. 2021b)
  - Ventilator-induced injury (Zhang et al. 2020a)

- HFNC mode (-flow)
  - Heat-related discomfort (Agarwal et al. 2020)
  - Mild altered level of consciousness (Agarwal et al. 2020)*
  - Thoraco-cervical discomfort (Agarwal et al. 2020)

Mild altered level of consciousness: The manufacturer does not consider this side effect to be directly related to HFNC therapy but rather the illness itself (ie. COVID-19). Thus, this risk shall not be added to the risk analysis file nor the IFU. Nevertheless, during all future updates this specific side effect shall be carefully monitored in the literature and added to the appropriate document if deemed necessary.*

Thus, no new contraindications nor adverse events have been identified, the manufacturer's information materials are consistent with the literature.

8.1.6 Preclinical data

The **EO-150 ventilator** must meet certain standards to ensure the safety of all patient population (adult and paediatric) therefore preclinical data has been carried out by EOVE which includes ;

- biocompatibility tests ("**100_69 C (p) Biocompatibility evaluation plan**", "**100_69 C (r) Biocompatibility evaluation report**" and "**100_79 H - Raw materials & critical components list**"):
    - direct-contact components: The materials in direct contact with the user are concerned by a limited exposure to the users' skin as defined in the norm 10993-1. The materials are well known and widely used for everyday life and thus, their biocompatibility is deemed appropriate for all populations of patients.

    - indirect-contact (air pathway) components: air pathway components are either Food contact grade or Medical contact grade (ISO 10993-1 and USP class VI). The biocompatibility of the **EO-150 ventilator** airway components is validated as the following standards have been validated by appropriate tests : Biocompatibility evaluation of breathing gas pathways (ISO 18562-1), Emission of particulate matter (ISO 18562-2) and mission of volatile organic compounds (ISO 18562-3). Therefore, the manufacturer can consider the complete air pathway of the **EO-150 ventilator** is safe for the user in terms of biocompatibility and cytotoxicity.

- Manufacturing and processing of the device: The chemicals used for manufacturing are either not in contact with the gas pathway (i.e. glues) or are biocompatible (i.e. disinfectants, silicon, etc.) and thus, are safe for all populations of patients.

- Mechanical, physical and electrical preclinical tests*: v*entilation sound pressure is compliant (ISO80601-2-72 standard), electromagnetic emissions and immunity tests are compliant (IEC 60601 level) and safe for all patient populations.

- Stability: the product has a shelf life of 10 years and is deemed safe for both adult and paediatric patients (see file "**100_616_B_lifetime evaluationEO150**").

- Container-Content Compatibility: the container-content compatibility is conform to the norm ISO 10993, based on the material datasheet and/or certificate given by the supplier and therefore safe for all groups of patients.

Thus, preclinical testing shows that the **EO-150 ventilator** is safe with regards to biocompatibility, manufacturing and processing steps, stability, container-content compatibility, mechanical and physical properties as they all comply with the appropriate norms and are deemed safe for both adult and paediatric patients.

In conclusion, the safety claimed for the **EO-150 ventilator** is supported with sufficient evidence from a variety of sources. Indeed, the safety of use for adult and children patients at home, as well as the manageable risks have been shown by the State of the Art, risk management, PMS and vigilance data. Of these identified risks, all are already known to the manufacturer and included in the manufacturer's risk analysis. Moreover, the manufacturer has implemented multiple alarms and back up modules according to appropriate standards, to safeguard against sudden device malfunction and/or shutdown. The **EO-150 ventilator** is considered compliant with MDR GSPR 1: Requirement on safety and MDR GSPR 4 : Requirement on safety..

8.2 SUMMARY OF CONFORMITY ASSESSMENT OF PERFORMANCE (GSPR 1)

The technical performance of the **EO-150 ventilator** is supported by data from :

- evaluation of a complete State of the Art,
- Usability tests,
- pre-clinical data of the device (see section H).

The technical performances claimed by EOVE for the **EO-150 ventilator** are the following:

- Compliant with performance standard : ISO 80601-2-72:2015
- Ensure an airflow between 1 and 60 L/min
- Ensure a volume between 30ml to 2.5 L
- Ensure a set insufflation pressure between 5 and 49 mb
- Ensure a set exhalation pressure between 1 and 25 mb
- Ensure a minimum breath rate of 5 to 80 c/min
- To set off appropriate alarms according to ISO 80601-2-72:2015 (see section 10.1.5.2.)

Main criteria used to evaluate the performance level of the **EO-150 ventilator** device was the capacity to correctly distribute air and/or gas to patients, in accordance with appropriate standards.

8.2.1 State of the Art

The use of MV to treat respiratory failure has been described since the 1960s. This well-established and managed treatment is now transposable to a home setting which has been shown to further improve performance.
The **EO-150 ventilator** technical performances are in line with articles from the literature used for performance data in terms of ventilation modes and settings (airflow, volume, insufflation/exhalation pressure) (see section 3.10.4.9.4.).

8.2.2 Preclinical data

The preclinical data demonstrates that the main performance criterion is reached, *ie.* settings are in accordance with the following standards:

- **ISO 80601-2-72:2015** : Compliance with this standard ensure the device meet required performance in terms of :
    - adjustable or calculated threshold of ventilation settings - "**100-19 specification motherboard software"**
    - essential performances, verifications procedures and usability safety tests of alarms **" report ISO 80601-2-72 n°13334266-775156-D-LCIE"** 31/08/2022

- **IEC 60601-1-8 / A2: 2020**: General requirements, tests and guidance for the alarms implemented on the device.

This shows that the **EO-150 ventilator** has the appropriate performance features and that suitable safeguard measures have been implemented to ensure patient safety and the correct performance of the device.

It can be concluded from these results that the **EO-150 ventilator** achieves its intended technical performance during normal conditions of use and that the intended performance is supported by sufficient technical evidence. On account of the rich State of the Art around HMV performance and the preclinical data that ensures the device has appropriate alarms and settings in terms of essential performances, verifications procedures and usability (see section 10.1.5.2.), the **EO-150 ventilator** is considered compliant with MDR GSPR 1: Requirement on safety and performance.

8.3 SUMMARY OF CONFORMITY ASSESSMENT ON ACCEPTABLE BENEFIT / RISK RATIO PROFILE (GSPR 2 and GSPR 8)

In order to determine the benefit/risk ratio profile, the technical performance of the **EO-150 ventilator**, supported by a complete State of the Art and pre-clinical data, and benefits are weighed against the risks reported in the :

- terms of use information (IFU and usability reports);
- risks report.

The **EO-150 ventilator** has no direct clinical benefit. The clinical benefit to the patient is related to the medical gas/air blend delivered to the patient - *i.e*. the ventilation therapy that is applied. As the ventilator assists in the mechanical delivery of ventilation therapy, the ventilator has an indirect patient benefit.

8.3.1 Terms of use

The IFU provides a detailed operative principle for the use of the device. The posology reported in the IFU for children weighing at least 3.5kg (8lbs) and adults, is similar to posologies reported in the State of the Art on similar devices for these populations. No unintended uses or "off-label" uses were reported (for both conventional and high-flow ventilation modes, see section 3.10.5.4.).

Moreover, the usability of the **EO-150 ventilator** was assessed reviewing the complaints received by EOVE via its usability studies, PMS monitoring, and vigilance data from international databases regarding the device and similar ones. The reports found in the different databases regarding the **EO-150 ventilator** and similar devices were mostly about the following issues:

- Cyber security measures (**EO-150 ventilator**);
- Internal battery preventative safety measures (**EO-150 ventilator**);
- Wireless connection loss without automatic restauration (**EO-150 ventilator**);
- Software/firmware issues (alarm triggers, keyboard, wrong settings, battery life indicator wrong, …) (**EO-150 ventilator** and similar devices);
- Manufacturing errors (moulding, assembly) (similar devices).

These incidents can be hazardous to patient health but all the issues mentioned are well-known and corrective actions were put in place by EOVE to resolve or limit their impact.
Moreover, performance and safety of the **EO-150 ventilator** can also be assessed in terms of usability by formative studies carried out on all types of **EO-150 ventilator** users. These showed that whilst using the latest version of the **EO-150 ventilator,** minor errors were made by users. But all tests were passed thus, the usability of the device as well as the information provided by the manufacturer allow for correct use of the device and thus, reached its expected performance.

The essential safety and performance requirements of the device are met in accordance with the analysis of incidents and complaints from the field, the risk management report and positive benefit-risk conclusions (see section 7).
Given that EOVE is aware of the risks associated with **EO-150 ventilator** and similar devices, the measures put in place to reduce these risks to as low as level as possible and the resulting absence of residual risks calculated by the risk management plan; EOVE has deemed there was no need for further user testing as the device is considered safe for use.

8.3.2 Risks

The risk analysis performed for the **EO-150 ventilator** showed that, after risk management, all **8** residual risks are accepted with the addition of warnings in the user manual. The updated risk analysis "**100_017 rev AI"** and

new **"100_813 rev B Cybersecurity Risk Analysis"** did not identify new residual risks and so the global residual risk remains acceptable.

No new risks were identified in the literature that require an update of the risk management file. Likewise, no new risks were identified from the international materiovigilance database search as well as in the PMS data, and no new usability issues were identified in the latest risk management file "**100_017 rev AI".**

8.3.3 Patient benefits

The **EO-150 ventilator** has no direct clinical benefit. The clinical benefit to the patient is related to the medical gas/air blend delivered to the patient - *i.e*. the ventilation therapy that is applied. As the ventilator assists in the mechanical delivery of ventilation therapy, the ventilator has an indirect patient benefit.

The use of MV to treat respiratory failure has been described since the 1960s. This well-established and managed treatment is now transposable to a home setting with no damaging effect to the patients' health. This explains why HMV is now recommended by guidelines to treat the most common diseases needing MV such as COPD (COPD Working Group 2012; Ergan et al. 2019; HAS, COPD care guideline 2019), NMDs (HAS, recommendations for HMV in NMDs 2006) and OHS (NICE Guideline for OSAHS and OHS 2021). HMV has important benefits to the patient, including improved $PtCO_2$, $PaCO_2$ levels, QoL, improved respiratory compliance and lowers costs, needs for IV as well as exacerbation frequency for COPD patients. **However, this benefit is indirectly attributed to the ventilator and directly associated with the air or medical gas/air blend provided to the patient.** All selected papers from the State of the Art unanimously state that HMV further benefits the patient compared to those treated with MV in hospitals. Adverse events reported for HMV (discomfort, oro-nasal dryness, skin lesions, dyspnoea and claustrophobia) are well known, manageable and largely outweighed by the benefits to the patient see section 3.10.4.9. for the full list). In all the indications included, patients' life quality and expectancy are substantially reduced when MV is refused. The benefit-risk balance is entirely in favour of HMV for the treatment of respiratory failure.

Thus, data from the risk analysis, international vigilance data, the State of the Art and clinical data on similar therapies showed that the majority of adverse events reported with the use of home mechanical ventilators are well-known, mitigated as much as possible and manageable. Moreover, the usability assessment of the **EO-150 ventilator** showed the occurrence of only minor errors or risks. Therefore, any risks associated with the use of home mechanical ventilators are acceptable when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety. The **EO-150 ventilator** is considered compliant with MDR GSPR 2: Requirement on benefit/risk ratio and MDR GSPR 8: any undesirable side-effect constitutes an acceptable risk when weighed against the intended performances.

9 CONCLUSION

9.1 COMPLIANCE WITH GENERAL REQUIREMENTS

The safety data of the **EO-150 ventilator** based on the State of the Art, risk analysis, PMS/PSUR activities and preclinical data have shown that the device is not associated with any novel contra-indications and agrees with the safety claims made by the manufacturer. Also, adverse events were reported in international databases but these are well-known to the manufacturer and managed via the risk analysis. The performance of the device under evaluation was supported by literature data (security, performance and patient benefits) and robust preclinical testing carried out by EOVE. Moreover, the acceptability of the benefit/risk ratio is favourable as per the usability assessment, the lack of new or residual risks after mitigation and patient benefits. Altogether, the level of evidence is sufficient to support the overall safety and performance of **EO-150 ventilator**.

The evidence presented and reviewed above are found acceptable and meet MDR general requirements GSPR1, GSPR2, GSPR4 and GSPR8 as specified in MDR 2017/745. The evidence supports the performance and safety of the **EO-150 ventilator** when used under normal conditions of use. All associated risks are deemed acceptable.

9.2 COMPLIANCE OF INFORMATION MATERIALS

The information materials provided by EOVE with **EO-150 Ventilator** comply with the information found in PMS data, vigilance data and the State of the Art (complications, side effects and contraindications). Therefore no modifications of the IFU and manufacturer materials are necessary.

9.3 RESIDUAL RISKS AND UNCERTAINTIES, UNANSWERED QUESTIONS

The benefit – risk ratio for **EO-150 Ventilator** is considered favourable, based on the conclusions reported above. The risk management report ("**100_67 - rev I - Risk management report"**) demonstrates that all residual risks are accepted and neither the State of the Art, the PMS data nor materiovigilance data found new risks, uncertainties or unanswered questions that require additional data or information.

No other remaining uncertainty or unanswered question remain to be answered by EOVE.

10 SECTION H: IF THE DEMONSTRATION OF COMPLIANCE BASED ON CLINICAL DATA IS NOT CONSIDERED APPROPRIATE (MEDDEV 2.7/1 REV. 4 UNDER DIRECTIVES 93/42/EEC OR 90/385/EEC A GUIDE FOR MANUFACTURERS AND NOTIFIED BODIES (JUNE 2016))

This CER is written in conformity with the requirements of the MDR 2017/745.

The **EO-150 ventilator** is CE-marked since 2015. According to Rule 12 of Annex VIII of MDR 2017/745, the **EO-150 ventilator** is a class IIb Medical Device that is not in direct contact with the patient. Therefore, the benefits to patients are indeed indirect; as the direct benefits are attributed to the air or gas/air blend administered to the patient.

According to Section 2 of Chapter I of MDR 2017/745, clinical evaluation is the analysis of "information relating to the safety or performance obtained in the use of a device from the following sources...":

- the clinical investigation(s) of the device concerned,
- the clinical investigation(s) or other studies cited in scientific publications of a device whose equivalence to the device concerned can be demonstrated,
- reports in peer-reviewed scientific publications on any other clinical experience with the device concerned or with a device whose equivalence to the device concerned can be demonstrated,
- clinically relevant information from post-market surveillance (PMS), in particular post-market clinical monitoring;".

However, Section 61, paragraph 10 of Chapter VI of MDR 2017/745 states: *Without prejudice to paragraph 4, where compliance with the general safety and performance requirements is considered not to have been satisfactorily demonstrated by clinical data, an appropriate justification shall be provided for any such exceptional case based on the results of the manufacturer's risk management and review of detailed data relating to the interaction between the device and the human body, the expected clinical performance and the manufacturer's claims. In this case, the manufacturer shall duly justify in the technical documentation referred to in Annex II why he considers adequate a demonstration of compliance with the general safety and performance requirements*

based solely on the results of non-clinical test methods, such as technical performance evaluation, bench testing and pre-clinical evaluation.

This justification enables the writing of a clinical evaluation without clinical performance data.
The manufacturer EOVE claims solely technical performances for the **EO-150 ventilator**.

Hence, the clinical evaluation related to EOVE **EO-150 ventilator** is based on the following combined data:

- Complete State of the Art;
- A description of the risks associated with the use of the medical device;
- Complications associated with the device;
- Complaints and vigilance, curated data;
- Compliance to non-clinical elements of common specifications considered relevant to device safety and performance, if applicable;
- Pre-clinical and bench testing / compliance to standards, if applicable.
- Clinical data retrieved on **EO-150 ventilator** from the scientific literature

Moreover, EOVE commits to perform PMCF in order to obtain data concerning the devices evaluated (APPENDIX 3: PMS / CLINICAL / BIOLOGICAL PLAN and "**100_881 rev B : PMCF_plan_EO-150"**).

The EOVE **EO-150 ventilator** can be considered as a device based on technologies with well-established safety and performance characteristics as it has common and stable design with little evolution. Its generic device group standard of care for respiratory failure and has well-known safety and clinical performance characteristics. There has been little evolution in its long history on the market in terms of indications and use according the State of the Art literature.

10.1 PRECLINICAL TEST

Preclinical tests are described in this chapters to complete the clinical evaluation of **EO-150 ventilator.**

10.1.1 Biocompatibility

The biological safety report of the **EO-150 ventilator** is available in the document **"100_613 Rev F"**: Annexe I of the 2017/745 regulation "**100_69 Rev C - Biocompatibilty evaluation report EO150**" and "**100_79 H - Raw materials & critical components list".**

10.1.1.1 Direct contact components

The user can have a direct contact with the **EO-150 ventilator**. The direct contact consist in a direct contact on the user intact skin by:

- Touching briefly the device User Interface;
- Taking the device by the handle;
- Touching briefly the keyboard;
- Extracting the module from the station.

These contacts are brief and lead to a limited exposure to the materials of the screen and of the handle. It correspond to a contact duration of less than 5 minutes cumulated in one day.
On the other side, the patient circuit composed of a tubing and of the final interface (*e.g.* Tracheotomy tube, mouthpiece, facial mask) is the item connected to the device output. Those items are not supplied by EOVE and the users purchase them themselves through their provider. The user manual requires these components to be CE marked to ensure biological safety.
The risk of a direct contact is evaluated in the product risk analysis file "**100_17 Risk Analysis Rev AI**" (Risks 94.2).

Raw material description of direct contact components

This material evaluation is used to identify all the possible biocompatibility-related hazards that might reach the patient during the use of the **EO-150 ventilator**.

In the table hereafter are listed the data collected on the different materials composing direct contact and critical components:

*Table 45: List of direct contact and critical components of the **EO-150 ventilator** according to IEC standards*

Component/ Part No.	Manufacturer/ Trademark	Type No./model No./	Technical data	Standard No./, Edition	Mark(s) & Certificates of conformity
Power supply	MASCOT	Type 2440	100-240VAC 50-60Hz 1,6A Output 28VDC ; 2,5A Class II PS ; IP41	IEC 60601-1	cURus E356182
European Power supply cord	FELLER	XVIH05VVH2F2 X075-C7W/1,80M SW9005 L37	Plug type XVI, 2,5A 250V	EN50075	ENEC 11
			Cord type H05VVH2F2X0, 0,75mm²	EN 50525:2011 EN 50525-2-11:2011 EN 50395:2005 + A1:2011 EN 50396:2005 + A1:2011	HAR, OVE
			Connector Type C7W 2,5A 250V	EN60320-1:2015 UL817 C22.2 No.21, JIS C8303	ENEC 11
US CA power cord	FELLER	Plug NEMA 1-15 Cord SVT2X18AWG Connector C7W	1,80m, black 7A/125V AC	UL 62 IEC 60320	UL, CSA
JP power cord	FELLER	Plug N1/15J Cord VCTFK 2x0,75 Connector C7	2,5m, black 7A/125V AC	JIS C 8303 JISC 3306	PSE (JET)
EO-150 Ventilator module, REF EO-VM150					
Plastic enclosure	ALBIS PLASTIC GMBH	KR2867 CWU	Acrylonitrile Styrene Acrylate/Polycarbonate (ASA/PC) V-0 for 1,5mm	IEC 60695- 11-10 UL 94	cURus E80168
Wiring	ALPHA WIRE CO	2842/7	PTFE insulation 28AWG VW-1 ; 80°C	UL 758	UR E163869
Connectors	JAPAN SOLDERLESS TERMINAL MFG CO LTD	B6B-ZR-SM4-TF	V-0	UL 1977	UL E60389

Component/ Part No.	Manufacturer/ Trademark	Type No./model No./	Technical data	Standard No./, Edition	Mark(s) & Certificates of conformity
Connectors	MOLEX	53398 series 53398-0871 53398-0471 548190572 22122104 - 7478 526101033 53398-0671 436500326 22-23-2041 - 6373	V-0	UL 1977	UR E29179
Connectors	SAMTEC INC	TFM-107-01-S-DRA SFM-107-02-S-D TFM-107-01-S-DRA TFM-107-02-S-D	V-0	UL 1977	UR E111594
+ PCB	SUNSHINE GLOBAL CIRCUITS CO LTD	All types	V-0	UL 94 UL 796	UR E229342
	SUNTAK MULTILAYER PCB CO LTD	SMT-5	V-0 ; 130°C	UL 94 UL 796	cURus E207844
Battery Li-ion	VLAD	EOVE 3 – 6INR19/66 6S1P Li-Ion	Li-ion : 21,6V – 2.95Ah – 63.7 Wh Cells SAMSUNG INR18650-30Q	IEC 62133-2	LCIE Test report 166234-748670 B
Primary battery	PANASONIC	CR1220	3V Max abnormal charging current 3mA	UL 1642	UR MH12210
Motor	ELECTROM AG	200A0138A	24 Vdc, 4,8 W	IEC 60601-1	Tested in this test report
Docking Station EO-AX0, REF EO-DCK1SLT					
Plastic enclosure	ALBIS PLASTIC GMBH	KR2867 CWU	Acrylonitrile Styrene Acrylate/Polycarbonate (ASA/PC) V-0 for 1,5mm	IEC 60695-11-10 UL 94	cURus E80168
+ Main board PCB	KUNSHAN SUHANG CIRCUIT BOARD CO LTD	SH-M1	V-0 ; 105°C min	UL 94 UL 796	UR E154554
+ wifi board	KUNSHAN SUHANG CIRCUIT BOARD CO LTD	All types	V-0 ; 105°C min	UL 94 UL 796	UR E154554
	SAFE COMPANY LTD	SAFE-4	V-0, 130°C	UL 94 UL 796	cURus E357349
Primary battery	PANASONIC	CR1220	3V Max abnormal charging current 3mA	UL 1642	UR MH12210
Electric fan	SUNONWEALTH ELECTRIC MACHINE INDUSTRY CO LTD	MC35100V2	DC5V 0,38W	UL 507	cURus E77551

Component/ Part No.	Manufacturer/ Trademark	Type No./model No./	Technical data	Standard No./, Edition	Mark(s) & Certificates of conformity
Connectors	HIROSE ELECTRIC CO., LTD.	HIROSEDF63SF_3PTS	V-0	UL 1977	UR E52653
Connectors	SAMTEC INC	SAMTEC_BTH-70P	V-0	UL 1977	UR E111594
Connectors	TE CONNECTIVITY INDUSTRIAL GMBH	M.2_PCI.E	V-0	UL 1977	UR E247738
Connectors	JAPAN SOLDERLESS TERMINAL MFG CO LTD	NSH series	V-0	UL 1977	UL E60389
Connectors	WUERTH ELEKTRONIK EISOS GMBH & CO. KG	USB_MICRO-AB-5	V-0	UL 1977	UR E323964
Connectors	AMPHENOL LTW TECHNOLOGY CO LTD	EMBA_000014_A 87520-0010BLF	V-0	UL 758	UR E489039

Evaluation of materials in direct contact with the user

The materials in direct contact with the user are concerned by a limited exposure to the users' skin as defined in the norm 10993-1 : 2018*. The materials are well known and widely used for everyday life. The PC-ASA is used for household object and also automobile interior. Polyester are widely used in the textile industry. The foreseen contact type for these materials are not different than the contact happening in the other known applications in the everyday life.
Therefore, the manufacturer can conclude that the information on these materials are sufficient to assess the safety of the direct contact of the user with them, in the scope of direct contact defined previously. No further evaluation of the material following 10993 norm is needed.
See files "**100_69 C (p) Biocompatibility evaluation plan**" and "**100_69 C (r) Biocompatibility evaluation report**".

** ISO 10993-1 : 2018 : « Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process».*

10.1.1.2 Indirect contact components

Some components of the **EO-150 ventilator** have indirect contact with the patient. Indeed, the air insulated by the **EO-150 ventilator** is in contact with several materials composing the inside air pathway:

- Air inlet filter cover;
- Foam filter;
- Blower;
- Flow sensor;
- Output to patient insufflation.

These materials can lead to hazardous situation if leachables come out of it and go in contact with the patient air pathway and in the worst case, are stored within the lung tissues.
The **EO-150 ventilator** can be used up to 24/24h by the patient. It corresponds to a permanent contact, as defined in the ISO 18562-1.
The hazards related to gas pathways biocompatibility are identified in the risk analysis of the product "**100_17 Risk Analysis Rev AI**" (Risks 94 and 94.1).
Therefore a biocompatibility evaluation of the breathing gas pathway following the norm 18562-1 is necessary to ensure safety of the **EO-150 ventilator** in terms of biocompatibility.

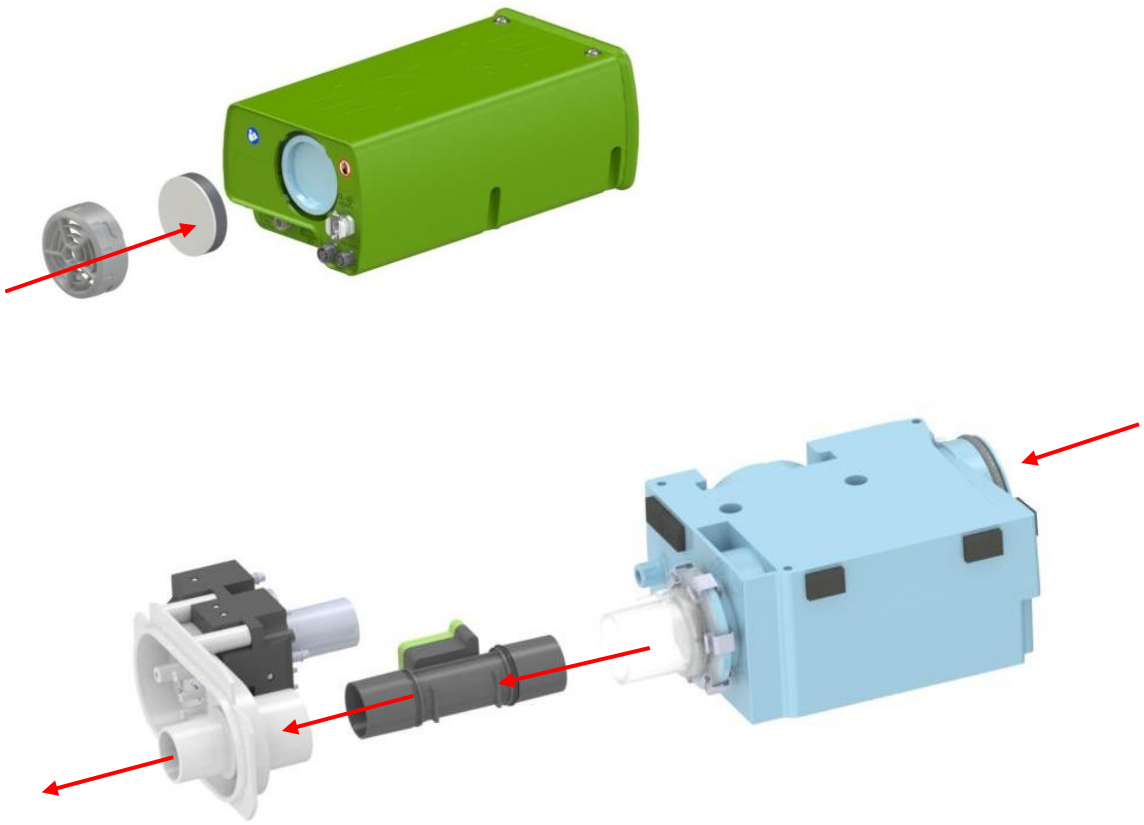


*Figure 47: Representation of airflow through the **EO-150 ventilator** module*

Raw material description of indirect contact (air pathway) components

This material evaluation is used to identify all the possible biocompatibility-related hazards that might reach the patient via the gas pathways during the use of the **EO-150 ventilator**.

In the table hereafter are listed the data collected on the different materials composing the air pathway of the **EO-150 ventilator**:

*Table 46: Raw materials of **EO-150 ventilator** air pathway*

Component	Material category	Material name	Comment
Air input part	ABS	Terluran GP-22	FDA and CE Food contact grade
	Colour	M203440	FDA and CE Food contact grade
Insufflation port part	ABS	Terluran GP-22	FDA and CE Food contact grade
	Colour	M08068B26	FDA and CE Food contact grade
Turbine - volute	Plastic	PC MAKROLON 2458	ISO 10993 and USP class VI

Turbine - impeller	Polayaryletherketone	PEEK 450 G Natural	EN 10204 - FDA Food contact grade
Turbine - casing	Plastic	PC MAKROLON 2458	ISO 10993 and USP class VI
	Colour	MEVOPUR 3%	ISO 10993 and USP class VI
Turbine - silicon part	Silicone	SILPURAN 4200	ISO 10993 and USP class VI
Turbine - foam	Polyether	REGISEAL TN 30 FR	NA

Note: The material data sheets are recorded in attachment 1 of the file "**100_69 Rev C - Biocompatibilty evaluation report EO150"**.

The total area of internal gas pathway in contact with the gas delivered to the patient is 749 178 $mm^{2.}$

Evaluation of materials not in direct contact with the user

No material evaluation following the ISO 18 562 Standards exists yet in EOVE on a similar gas pathway.
By design, most of the materials used are not expected to lead to biocompatibility hazards, because they are either Food contact grade or Medical contact grade (10993-1 and USP class VI). To confirm biocompatibility of the **EO-150 ventilator** device, the following tests were conducted:

*Table 47: Preclinical biocompatibility tests for air pathway components of the **EO-150 ventilator***

Test specification	Standard	Report title
Biocompatibility evaluation of breathing gas pathways	**ISO 18562-1: 2017 :** Biocompatibility evaluation of breathing gas pathways in healthcare applications – Part 1: Evaluation and testing within a risk management process.	"**100_69 C (p) Biocompatibility evaluation plan**" and "**100_69 C (r) Biocompatibility evaluation report**" "+ external report "**ISO 18562-1 - Risk Assessment EO-150 n°1001565584-4974254BA"** – 27/09/2022
Emission of particulate matter	**ISO 18562-2 : 2017**: Biocompatibility evaluation of breathing gas pathways in healthcare applications – Part 2: Tests for emissions of particulate matter	"**ISO18652-2 report n° 1001600886-5077340P R1"** of 29/08/2022
Emission of volatile organic compounds	**ISO 18562-3 : 2017** : Biocompatibility evaluation of breathing gas pathways in healthcare applications – Part 3: Tests for emissions of volatile organic compounds (VOCs)	"**ISO18652-3 report n°1001565584-4974254"** of 25/08/2022
The emission of leachable in condensate	**ISO 18562-4 : 2017** : Tests for Leachables in Condensate	Not applicable*

* No condensates are present during normal use of the **EO-150 ventilator**.

All the tests carried out show compliance of the airway components of the **EO-150 ventilator** to applicable biocompatibility standards mentioned above. The manufacturer can therefore consider that the re-dropped chemical compounds are negligible and without risk to the patient. In conclusion, the complete air pathway of the **EO-150 ventilator** is not expected to cause hazardous situation to the device user. The **EO-150 ventilator** is safe for the user in terms of biocompatibility and cytotoxicity.

10.1.2 Manufacturing facilities and processes biocompatibility

The materials and chemical used for the manufacturing of the **EO-150 ventilator** were evaluated based on the available documentation (date sheets, FDS, internal documentation,...) in the biocompatibility evaluation plan "**100_69 C (p) Biocompatibility evaluation plan**".

In the table hereafter are listed the data collected on the chemicals used for the manufacturing of the **EO-150 ventilator**:

*Table 48: Chemicals used for the manufacturing of the **EO-150 ventilator***

Manufacturing product designation	Processing product name	MSDS (on Drive EOVE_PRODUCTION/Produits chimiques/...)
Surface disinfection	Cleaner VHB 3M	FDS Cleaner VHB.pdf
Thread Lock	Loctite 222	FDS Loctite 222.pdf
Turbine sealing glue	Silicone Elastosil E41	FDS Elastosil E41.pdf
Suppliers manufacturing chemicals		
Surface cleaning (pneumatic bloc)	Common dishwasher detergent	NA

The incorrect use of these chemicals during production, which could lead to a biocompatibility risk, are identified in the manufacturing AMDEC **(FAB100_002**) with risks 12, 12 bis, 131 bis, 133 bis and 465.

In conclusion, the chemicals used for manufacturing are either not in contact with the gas pathway (*i.e*. glues) or are biocompatible (*i.e.* disinfectants, silicon, etc.).

10.1.3 Disinfection of the device

In the table hereafter are listed the data collected on the chemicals used for processing the **EO-150 ventilator**:

*Table 49: chemicals used for the processing of the **EO-150 ventilator***

Processing product designation	Processing product name	MSDS
Surface disinfection	Cleaner VHB 3M	FDS Cleaner VHB.pdf
Surface disinfection	Reztore	FDS Nettoyant ESD Reztore.pdf

In conclusion, the chemicals used for processing/disinfection are either not in contact with the gas pathway (*i.e.* glues) or are biocompatible (*i.e.* disinfectants, etc.).

10.1.4 Mechanical, physical and electrical preclinical tests

10.1.4.1 Performance report

A detailed account of the **EO-150 ventilator** performance report is available in the report file "**100_53 T(r)-Ventilation performance report**". Briefly, this report describes performance test results of the **EO-150 ventilator** with CPU software version C150000702, which integrated the performance report revision S and S-1.
Those performances deal with accuracy of settings and monitored parameters.

Ventilation module must meet the following performances for set parameters :

- Valve volumes: ± (5 ml + 10%) under BTPS conditions except in sigh mode
- Volumes (valve configuration in sigh mode) : ± (10ml +20%)

- Volumes (leak configuration) : ± (10 ml + 10%) BTPS conditions
- Volumes (MPV configuration) : ± (10 ml + 15%) BTPS conditions
- Pressures (plateau) : ± (1 mb + 10%)
- Times : ± 0.1 s
- Rates : ± 1 c/min
- Flows : ± (0.5 l/min + 10%)

The conclusion of the report states that all executed tests are passed within the tolerance.

10.1.4.2 Alarms and acoustic testing

Acoustic test results were in accordance with the ISO 80601-2-72 norm and are provided in the table below (For more information see test report number: 13334266-775156-D): Ventilation Sound Pressure weighted A. 45 dB +/- 10%

*Table 50: Acoustic test results for the **EO-150 ventilator** in 3 standard ventilation settings*

of the positions of the Microphones coordinates x, y, z (m) - Ten microphone position in a hemisphere radius as per ISO 3744:2010, clause 7.2.	**Sound power level (dB)** Calculated A-Weighted sound power level measurements. As per ISO 3744:2010, clause 8.6.	**Result - Remarks**	**Verdict** (P = pass)
Delivered volume 500ml, adult mode	46,39	None	P
Delivered volume 150ml, pediatric mode	46,53	None	P
Delivered volume 30ml, pediatric mode	46,04	None	P

The alarm on the **EO-150 ventilator** are a major safety aspect of the device. The manufacturer has implemented appropriate alarms according to the standard ISO 80601-2-72. The following table provides an overview of alarm essential performances but all other aspects regarding the alarms is provided in the report file "**Rapport ISO 80601-2-72 n°13334266-775156-D-LCIE -31 aout 2022**":

*Table 51: **EO-150 ventilator** alarm essential performance test results according to the ISO 80601-2-72 standard*

Essential Performances	**Risk Management Document Referenced** (Document No. & Clause)	**Result - Remarks**	**Verdict** (P = pass)
Delivery of ventilation at the PATIENT-CONNECTION PORT within the ALARM LIMITS set by the OPERATOR	ISO 80601-2-72, table 201.101	None	P
generation of an ALARM CONDITION AIRWAY PRESSURE	ISO 80601-2-72, table 201.101 Clause 201.12.4.102	None	P
generation of an ALARM CONDITION continuing positive-pressure	ISO 80601-2-72, table 201.101 Clause 201.12.4.110	None	P
generation of an ALARM CONDITION DELIVERED VOLUME	ISO 80601-2-72, table 201.101 Clause 201.12.1.104	None	P
generation of an ALARM CONDITION high AIRWAY PRESSURE	ISO 80601-2-72, table 201.101 Clause 201.12.4.106	None	P
generation of an ALARM CONDITION hypoventilation	ISO 80601-2-72, table 201.101 Clause 201.12.4.109	None	P

generation of an ALARM CONDITION INTERNAL ELECTRICAL POWER SOURCE nears depletion	ISO 80601-2-72, table 201.101 Clause 211.8.4.101	None	P
generation of an ALARM CONDITION high leakage	ISO 80601-2-72, table 201.101 Clause 201.12.4.111	None	P
generation of an ALARM CONDITION low expired volume	ISO 80601-2-72, table 201.101 Clause 201.12.4.103	None	P
generation of an ALARM CONDITION obstruction	ISO 80601-2-72, table 201.101 Clause 201.12.4.107	None	P

10.1.4.3 Electromagnetic emissions

Table 52: Electromagnetic emissions tests

Emissions test	Level of compliance	Guidance for EM environment
RF emissions CISPR 11	Class B	EO150 is suitable for home health care environment and a professional health care establishment
Harmonic Emissions IEC 61000-3-2	Complying	
Voltage Fluctuations/Flicker Emissions IEC 61000-3-3	Complying	

Table 53: Electromagnetic immunity tests

Immunity Test	IEC 60601 level	Level of compliance	Guidance for EM environment
Electrostatic discharge (ESD) IEC 61000-4-2	8 kV contact 15 kV air	8 kV contact 15 kV air	for home health care environment and a professional health care establishment
Electrical fast transient/burst IEC 61000-4-4	2 kV for power supply lines 1 kV for input/output lines	2 kV for power supply lines 1 kV for input/output lines	for home health care environment and a professional health care establishment
Surge IEC 61000-4-5	1 kV differential mode 2 kV common mode	1 kV differential mode 2 kV common mode	for home health care environment and a professional health care establishment
Voltage dips, short interruptions, and voltage variations on power supply input lines IEC 61000-4-11	0% Ut for 0.5 cycle With 0°, 45°, 90°, 135°, 180°, 225°, 270° and 315° 0% Ut for 1 cycles 70% Ut for 25 cycles at 50 Hz For 30 cycles at 60 Hz Monophased at 0°	0% Ut for 0.5 cycle With 0°, 45°, 90°, 135°, 180°, 225°, 270° and 315° 0% Ut for 1 cycles 70% Ut for 25 cycles at 50 Hz For 30 cycles at 60 Hz Monophased at 0°	Mains power quality should be as home health care environment and a professional health care establishment If operating during power cuts, it is recommended to use other power sources.
Voltage Interruption IEC 61000-4-11	0 % UT for 250 cycles at 50 Hz for 300 cycles at 60 Hz	0 % UT for 250 cycles at 50 Hz for 300 cycles at 60 Hz	

Immunity Test	IEC 60601 level	Level of compliance	Guidance for EM environment
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	30 A/m	30 A/m	for home health care environment and a professional health care establishment
Conducted RF IEC 61000-4-6	3 Vrms 150 kHz to 80 MHz 6 V in ISM band and from 0.15 MHZ to 80 MHZ, amateur radio band included 80% MA at 1 KHz	3 Vrms 150 kHz to 80 MHz 6 V in ISM band and from 0.15 MHZ to 80 MHZ, amateur radio band included 80% MA at 1 KHz	for home health care environment and a professional health care establishment
Electromagnetic fields Radiated RF* IEC 61000-4-3	10 V/m 80 MHz to 2.5 GHz	10 V/m 80 MHz to 2.5 GHz	for home health care environment and a professional health care establishment
Proximity fields emitted by RF wireless communication devices IEC 61000-4-3 (provisional method)	9 V/m: 710 MHz, 745 MHz, 780 MHZ, 5240 MHz, 5550 MHz, 5785 MHz 27 V/m: 385 MHz 28 V/m: 450 MHz, 810 MHz, 870 MHz, 930 MHz, 1720 MHz, 1845 MHz, 1970 MHz, 2450 MHz	9 V/m: 710 MHz, 745 MHz, 780 MHZ, 5240 MHz, 5550 MHz, 5785 MHz 27 V/m: 385 MHz 28 V/m: 450 MHz, 810 MHz, 870 MHz, 930 MHz, 1720 MHz, 1845 MHz, 1970 MHz, 2450 MHz	for home health care environment and a professional health care establishment

The tests are carried out by COFRAC accredited laboratories. (accreditation 17 025) which are monitored in the QMS. In particular for tests carried out in accordance with the following standards:

- IEC 60601-1 : 2012 + A2 2020 : test reports n° 13334266-775156-A of 31 August 2022
- IEC 60601-1-2 : 2014 : test report n° 12967369 -773197 dated 24 August 2022
- ISO 14971 : 2019 + A11 :2021 : report n°100_71 Rev C.
- IEC 62304 : 2006 + A1 2015 : report n°100_72 Rev C.
- IEC 60601-1-6 : 2010 + A1 2013 + A2 2020 : test report n°13334266-775156-B of 31 August 2022.
- IEC60601-1-8 : 2006 + A1 2012 : test report n° 162649-740083-C dated 20 March 2020 (LCIE).
- IEC 60601-1-9 2007 + A1 2013 : test report n°169649-742412 dated 18 March 2020 (LCIE).
- IEC 60601-1-11 : 2015 + A1 2020 : test report n° 13334266-775156-C of 31 August 2022.
- IEC 62366-1 : 2015 + A1 2020 : report n°100_74 Rev E.
- ISO 80601-2-72 : 2015 : test report n°13334266-775156-D of 31 August 2022
- IEC 62133-2 : 2017 : test report n° 166234-748670-B dated 29 May 2020 (LCIE).
- ISO 10993-1 : 2018 : report n° 100_69 (p) Rev.C + 100_69 (r) Rev.C
- ISO 18562-1: 2017: report no. 100_69 (p) Rev.C + 100_69 (r) Rev.C + external report ISO 18562-1 - Risk Assessment EO-150 n°1001565584-4974254BA - 27 sept 2022
- ISO 18652-2 : 2017 : report n° 1001600886-5077340P R1 of 29 August 2022
- ISO 18652-3 : 2017 : report n° 1001565584-4974254 of 25 August 2022
  ETSI EN 300 328 V2.1.1 (Directive 2014/53/EU: RED): test report no. 162649-740085-A of 26 November 2019 (LCIE).
- RTCA DO 160 G: test report no. 162649-740094 dated 7 Oct. 2019 (LCIE - EMC) + n°162649-740093 du 13 oct 2022 (LCIE - Mechanical).

10.1.5 Stability

All data relevant to device stability is detailed in the file "**100_616_B_lifetime evaluationEO150**" and carried out according to the following protocol:

The **EO-150 ventilator** is expected to be used at home or at the hospital for 16 hours per day. For the settings, two use cases are taken into account in this evaluation. They represent the setup which use the most the components for paediatric and adult patient. For each component, the evaluation of the shelf life is be done based on the worst use of the component.

- Adult case:
  The device is used continuously in a VAC mode with a rate of 15 breath/min, a Vt of 750 mL and a Pep at 0 mbar. The other parameters are at their default value. A double patient circuit with valve is used.
- Paediatric case:
  The device is used continuously in a VPC mode with a rate of 40 breath/min, a inhalation pressure of 18 mbar and a Pep at 5 mbar. A double patient circuit with valve is used.

Turbine and inspiration flow sensor are always on when device is on.
The electro valve is cycling once per breath.
In regards from these data, the expected use time for the component **in one year** are the following:

- Motor turbine MFA 0300I: 5 840 hours;
- Electro-valves: $14{,}016.10^6$ switches;
- Sensor inspiration flow: 5 840 hours;
- CPU Board: 5 840 hours.

*Table 54: **EO-150 ventilator** components shelf life validation*

Component	**Manufacturer shelf life indication**	**Maintenance associated measures**	**Expected use in maintenance time** (10 years if no maintenance)	**Manufacturer shelf life in line with maintenance recommendation ?** (Yes/No)
Motor turbine MFA0300 I Ref.: 200A0106 / 200A0106	> 40 000 hours (See attachment 3)	Replacement after 20 000/30 000 hours for paediatric/adult use	20 000/30 000 hours for paediatric/adult use	Yes
Electro valve Ref.: Preciflow LS202A515 24VDDC	MTBF > 100 millions cycles	Replacement after 100 millions cycles	100 millions cycles	Yes
Sensor flow Ref.: SFM3000-200-C	10 years (See attachment 1 for rational)	4 years	24 000 hours	Yes
CPU Board Ref.: CPU Board EO151	Internal development. MTBF test in attachment 2: Result = 80 000 hours	NA	58 400 hours	Yes
Keyboard Ref.: 544030 ENS C	Buttons: 500 000 pushes LEDs: 73 300 hours (See attachment 4)	NA	Buttons: 73 000 pushes LEDs: 58 400 hours	Yes
AC Connector Ref.: L722RAS	10 000 cycles connection/disconnection (See attachment 5)	NA	7 300 cycles	Yes

Component	Manufacturer shelf life indication	Maintenance associated measures	Expected use in maintenance time (10 years if no maintenance)	Manufacturer shelf life in line with maintenance recommendation ? (Yes/No)
Piston board connector Ref.: 811-S1-002-10-017101	50 000 cycles connection/disconnection (See piston technical sheet - attachment 6)	NA	7 300 cycles	Yes
GUI Tactile interface Ref.: UMOH-9597MD-1T	1 467 812 hours (see calculation note in attachment 7)	NA	58 400 hours	Yes

If the maintenance schedule of the **EO-150** device is correctly followed, the product has a shelf life of 10 years.

The flow sensor is manufactured by Sensirion. They stated that the SMF was designed to be used more than 10 years. Moreover they provide EOVE the stress test validation they performed on the sensors on which they based their assumption (see emails "**Sensirion-lifetimeSMF300.pdf**" and the validation report file "**GF_R_SFM3000_Qualification_Report_v1.3_D3.pdf**").

The CPU cards reliability study are detailed in the file "**EOV-Reliability study 0001 A.pdf**".
The shelf life study of the MFA030x is detailed in the file "**OENG-191009-NT-01-Extrapolation LT MFA030x Eove conditions.pdf**".
The shelf life calculations for the **EO-150 ventilator** display screen is detailed in the file "811-S1-002-10-017101.pdf".

10.1.6 Container-Content Compatibility

The container-content compatibility was taken into account during the design, the materials composing the air pathway were selected among plastic and materials for food usage, or conform to the norm ISO 10993, based on the material datasheet and/or certificate given by the supplier. The raw materials of those composing the air pathway are specified in the file "**100_79 H - Raw materials & critical components list"** but also appear in the table 3 and 49.
Moreover, there are no manufacturing residues.
The primary packaging material is the packing carton.

10.1.7 Conclusion

- ✓ ***Biocompatibility – direct contact components***

The materials in direct contact with the user are concerned by a limited exposure to the users' skin as defined in the norm **10993-1**. The materials are well known and widely used for everyday life. Their biocompatibility is deemed appropriate for all populations of patients (adult and paediatric).
See details in files "**100_69 C (p) Biocompatibility evaluation plan**", "**100_69 C (r) Biocompatibility evaluation report**" and "**100_79 H - Raw materials & critical components list**".

- ✓ ***Biocompatibility – indirect contact components (Air pathway)***

Although the **EO-150 ventilator** is not in direct contact with the patient, the device is in contact with the distributed air (or air/gas blend). Thus, air pathway components are either Food contact grade or Medical contact grade (**ISO 10993-1** and **USP class VI**). The biocompatibility of the **EO-150 ventilator** airway components is validated as the following standards have been validated by appropriate tests previously mentioned in section 10.1.1.2. :

- Biocompatibility evaluation of breathing gas pathways (**ISO 18562-1**)
- Emission of particulate matter (**ISO 18562-2**)
- Emission of volatile organic compounds (**ISO 18562-3**)

In conclusion, the manufacturer can therefore consider that chemical compounds released are negligible and without risk to the patient. Thus, the complete air pathway of the **EO-150 ventilator** is not expected to cause hazardous situation to the device user. The **EO-150 ventilator** is safe for the user in terms of biocompatibility and cytotoxicity.
See details in files "**100_69 C (p) Biocompatibility evaluation plan**", "**100_69 C (r) Biocompatibility evaluation report**" and "**100_79 H - Raw materials & critical components list**".

- ✓ ***Manufacturing facilities and processes biocompatibility***

Biocompatibility risk linked to incorrect use have been identified in the manufacturing AMDEC **(FAB100_002**) with risks 12, 12 bis, 131 bis, 133 bis and 465.

Moreover, the chemicals used for manufacturing are either not in contact with the gas pathway (*i.e.* glues) or are biocompatible (*i.e.* disinfectants, silicon, etc.).

- ✓ ***Disinfection of the device***

Moreover, the chemicals used for processing or disinfection are either not in contact with the gas pathway (*i.e.* glues) or are biocompatible (*i.e.* disinfectants, silicon, etc.).

- ✓ ***Performance report***

Performance tests of the **EO-150 ventilator** in terms accuracy of settings and monitored parameters were passed to meet the following performances for set parameters :

- Valve volumes: ± (5 ml + 10%) under BTPS conditions except in sigh mode
- Volumes (valve configuration in sigh mode) : ± (10ml +20%)
- Volumes (leak configuration) : ± (10 ml + 10%) BTPS conditions
- Volumes (MPV configuration) : ± (10 ml + 15%) BTPS conditions
- Pressures (plateau) : ± (1 mb + 10%)
- Times : ± 0.1 s
- Rates : ± 1 c/min
- Flows : ± (0.5 l/min + 10%)

- ✓ ***Alarms and acoustic testing***

The manufacturer has implemented appropriate alarms and verification procedures according to the standard **ISO 80601-2-72**.

- ✓ ***Electromagnetic emissions***

The electromagnetic emissions and immunity tests are compliant with all appropriate standards mentioned above.

- ✓ ***Stability***

Separate tests have been carried out for each component and both adult and paediatric conditions of use. If the maintenance schedule of the EOVE **EO-150 ventilator** device is correctly followed, the product has a shelf life of 10 years (See details in the file "**100_616_B_lifetime evaluationEO150**").

- ✓ ***Container-Content Compatibility***

The container-content compatibility was taken into account during the design, the materials composing the air pathway were selected among plastic and materials for food usage, or conform to the norm ISO 10993, based on the material datasheet and/or certificate given by the supplier.
Moreover, there are no manufacturing residues.

11 DATE OF THE NEXT CLINICAL EVALUATION

As described in the CEP ("**100_66 rev H : CEP_EO-150"**), a **2**-year update will be planned for the CER of the **EO-150 ventilator** (See APPENDIX 3: PMS / CLINICAL / BIOLOGICAL PLAN).

According to MEDDEV 2.7/1, this clinical evaluation shall also be actively updated:

- In case of a change of conception of the device that has the potential to modify its performance and safety; and
- If new information from PMS has the potential to change the current evaluation.

Date of the next version of the evaluation: November 2024

When updating the clinical evaluation, it should be verified:

- If the benefit/risk profile, undesirable side-effects (whether previously known or newly emerged) and risk mitigation measures are still:
  - compatible with a high level of protection of health and safety and acceptable according to the current knowledge/ State of the Art;
  - correctly addressed in the information materials supplied;
  - correctly addressed by the current PMCF plan;
- If existing claims are still justified;
- If new claims (if applicable) are justified.

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13 APPENDIX

Number of Appendix	Documents
1	CV of Authors, Reviewers and Approver
2	Declaration of interest
3	PMS / CLINICAL / BIOLOGICAL PLAN
4	State of the Art - Literature search
5	State of the Art - Literature selection
6	Vigilance data from international databases
7	Information supplied with the device
8	Biological risk assessment
9	Stability data
10	Risk management dossier

13.1 APPENDIX 1: CV OF WRITER, REVIEWERS AND APPROVER

See Electronic Appendix:

- DC_EFOR_RENAUD_SARAH_EN
- DC_EFOR_HOEGL_KATHARINA_EN
- DC_EFOR_BENOIT_CHARLOTTE_EN

13.2 APPENDIX 2: DECLARATION OF INTEREST

Clinical Evaluation Report: **EO-150 ventilator**

Following the MEDDEV 2.7/1 Rev. 4, MDR (EU) 2017/745 and GMED requirements

Name: Sarah RENAUD
Title: Consultant, EFOR Group

☐ YES ☒ NO	Time span (e.g. grants, sources of revenue or benefits paid or promised to be paid over the 36 months prior to the evaluation)
☐ YES ☒ NO	Financial interests of family members included or not (namely spouse or partner living in the same residence as the evaluator, children and adults for whom the evaluators is legally responsible)
☐ YES ☒NO	Employment by the manufacturer
☐ YES ☒NO	Participation as an investigator in clinical studies of the device, or in pre-clinical testing of the device
☐ YES ☒NO	Ownership / shareholding possibly affected by the outcome of the evaluation
☐ YES ☒NO	Grants sponsored by the manufacturer
☐ YES ☒NO	Benefits such as travelling or hospitality (if beyond what is reasonably necessary for the work as an employee or external evaluator)
☐ YES ☒NO	Interests in connection with the manufacturing of the device or its constituents
☐ YES ☒NO	Interests in connection with intellectual property, such as patents, copyrights and royalties (whether pending, issued or licensed) possibly affected by the outcome of the evaluation
☐ YES ☒NO	Other interests or sources of revenues possibly affected by the result of the evaluation

Eligibility of the writer for the signature of the CER:

☐ NO
☒YES
☐ YES with the following limitations:

Signature writer, date ***Signature manufacturer, date***
23/02/2023

Clinical Evaluation Report: **EO-150 ventilator**

Following the MEDDEV 2.7/1 Rev. 4, MDR (EU) 2017/745 and GMED requirements

Name: Katharina HOEGL
Title: Technical Specialist (EFOR Group)

☐ YES ☒ NO	Time span (e.g. grants, sources of revenue or benefits paid or promised to be paid over the 36 months prior to the evaluation)
☐ YES ☒ NO	Financial interests of family members included or not (namely spouse or partner living in the same residence as the evaluator, children and adults for whom the evaluators is legally responsible)
☐ YES ☒NO	Employment by the manufacturer
☐ YES ☒NO	Participation as an investigator in clinical studies of the device, or in pre-clinical testing of the device
☐ YES ☒NO	Ownership / shareholding possibly affected by the outcome of the evaluation
☐ YES ☒NO	Grants sponsored by the manufacturer
☐ YES ☒NO	Benefits such as travelling or hospitality (if beyond what is reasonably necessary for the work as an employee or external evaluator)
☐ YES ☒NO	Interests in connection with the manufacturing of the device or its constituents
☐ YES ☒NO	Interests in connection with intellectual property, such as patents, copyrights and royalties (whether pending, issued or licensed) possibly affected by the outcome of the evaluation
☐ YES ☒NO	Other interests or sources of revenues possibly affected by the result of the evaluation

Eligibility of the reviewer for the signature of the CER:

☐ NO
☒YES
☐ YES with the following limitations:

Signature reviewer, date ***Signature manufacturer, date***
23/02/2023

Clinical Evaluation Report: **EO-150 ventilator**

Following the MEDDEV 2.7/1 Rev. 4, MDR (EU) 2017/745 and GMED requirements

Name: Charlotte BENOIT
Title: Head of Clinical Department (EFOR Group)

☐ YES ☒ NO	Time span (e.g. grants, sources of revenue or benefits paid or promised to be paid over the 36 months prior to the evaluation)
☐ YES ☒ NO	Financial interests of family members included or not (namely spouse or partner living in the same residence as the evaluator, children and adults for whom the evaluators is legally responsible)
☐ YES ☒NO	Employment by the manufacturer
☐ YES ☒NO	Participation as an investigator in clinical studies of the device, or in pre-clinical testing of the device
☐ YES ☒NO	Ownership / shareholding possibly affected by the outcome of the evaluation
☐ YES ☒NO	Grants sponsored by the manufacturer
☐ YES ☒NO	Benefits such as travelling or hospitality (if beyond what is reasonably necessary for the work as an employee or external evaluator)
☐ YES ☒NO	Interests in connection with the manufacturing of the device or its constituents
☐ YES ☒NO	Interests in connection with intellectual property, such as patents, copyrights and royalties (whether pending, issued or licensed) possibly affected by the outcome of the evaluation
☐ YES ☒NO	Other interests or sources of revenues possibly affected by the result of the evaluation

Eligibility of the reviewer for the signature of the CER:

☐ NO
☒ YES
☐ YES with the following limitations:

Signature reviewer, date ***Signature manufacturer, date***
23/02/2023

13.3 APPENDIX 3: PMS / CLINICAL / BIOLOGICAL PLAN

See Electronic Appendix: [“**100_611 B - Plan de surveillance après commercialisation - EO-150**”, “**100_612 E**” - “**Rapport annuel de sécurité - PSUR EO-150”**, “ **100_881 rev B : PMCF_plan_EO-150”**

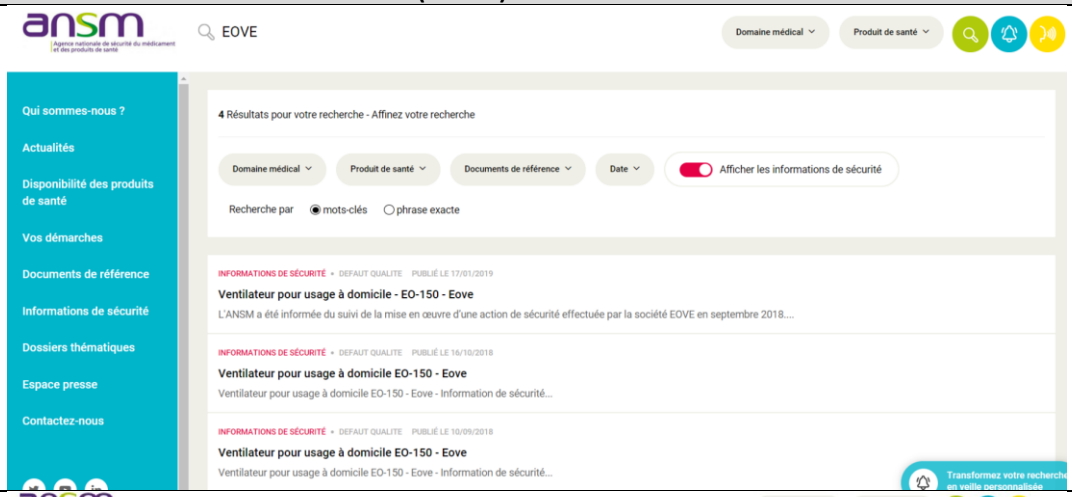
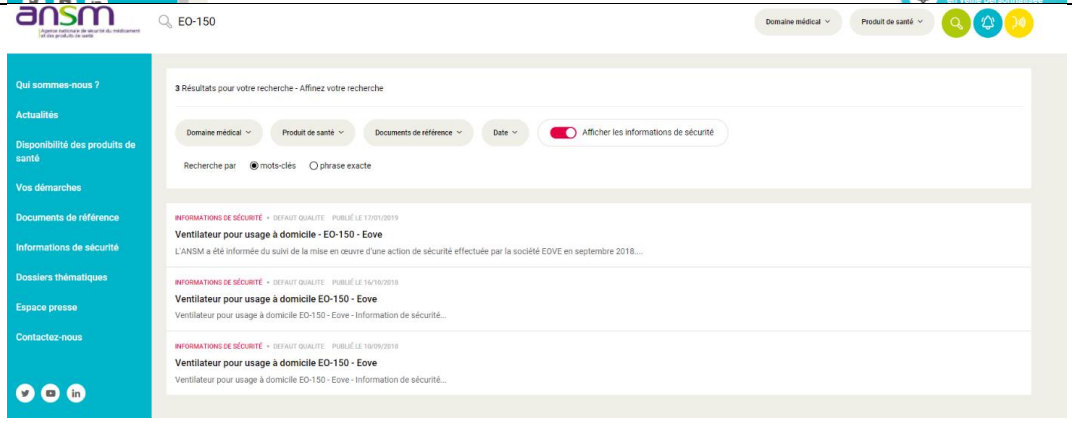
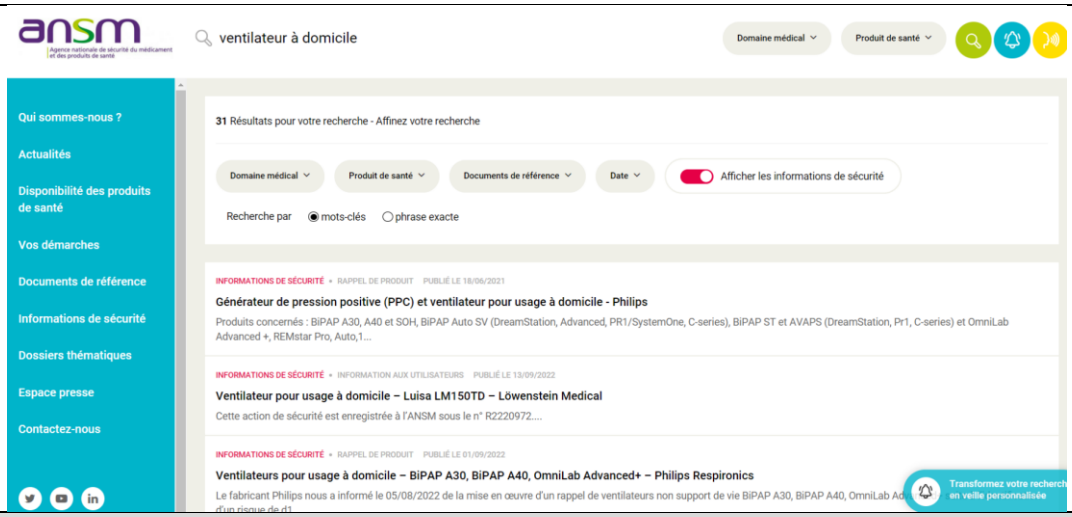
13.4 APPENDIX 4: STATE OF THE ART - LITERATURE SEARCH

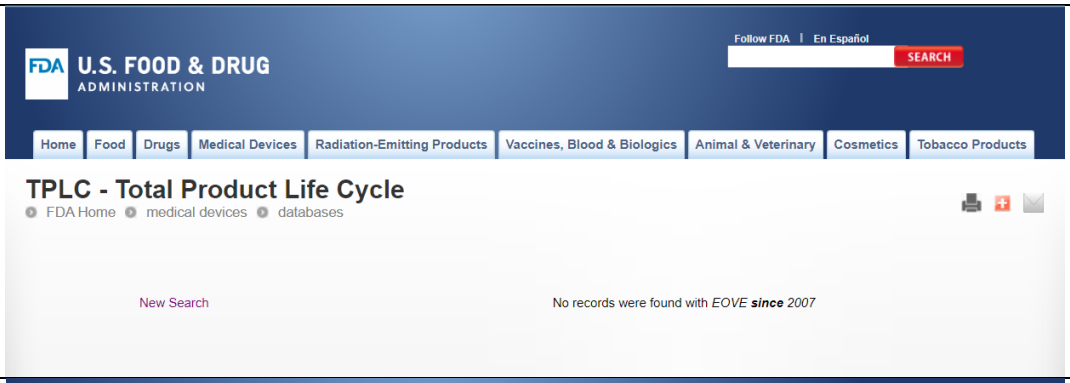
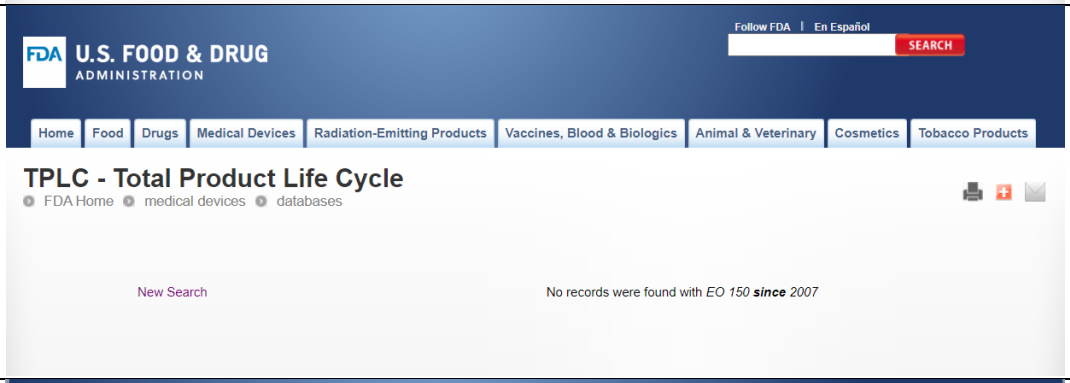
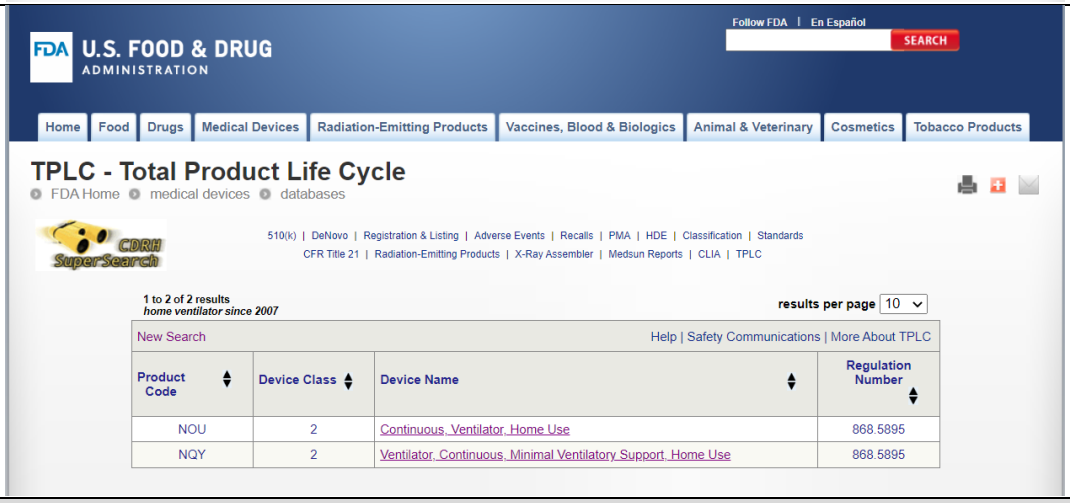
The literature selection for the State of the Art is available in the electronic appendix: "**100_66 rev G : EO-150_literature_search_protocol"**.

13.5 APPENDIX 5: STATE OF THE ART - LITERATURE SELECTION

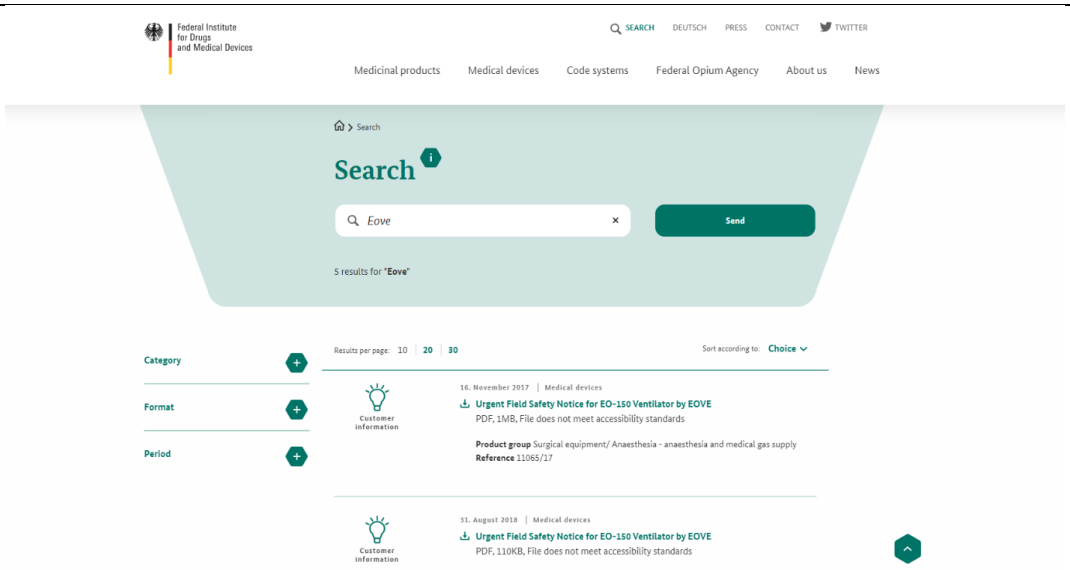
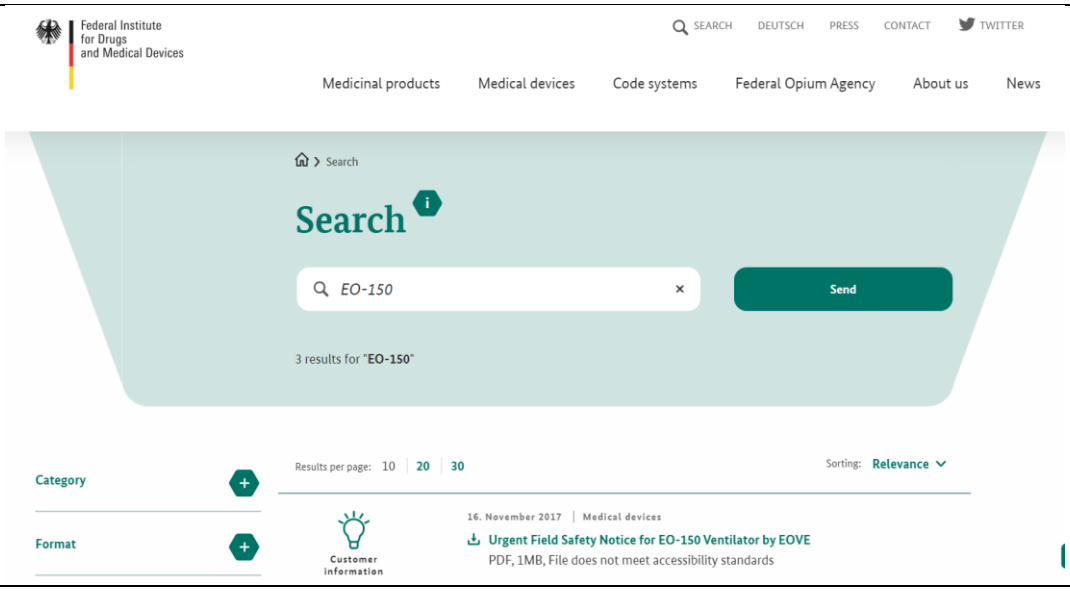
The literature selection for the State of the Art is available in the electronic appendix: "**100_66 rev G : EO-150_literature_search_report".**

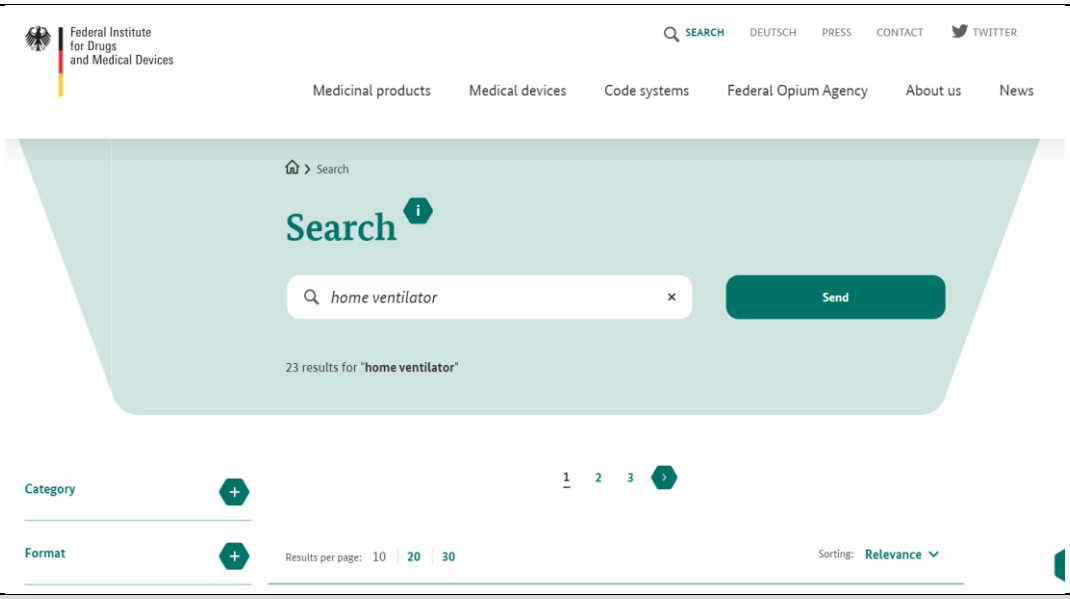
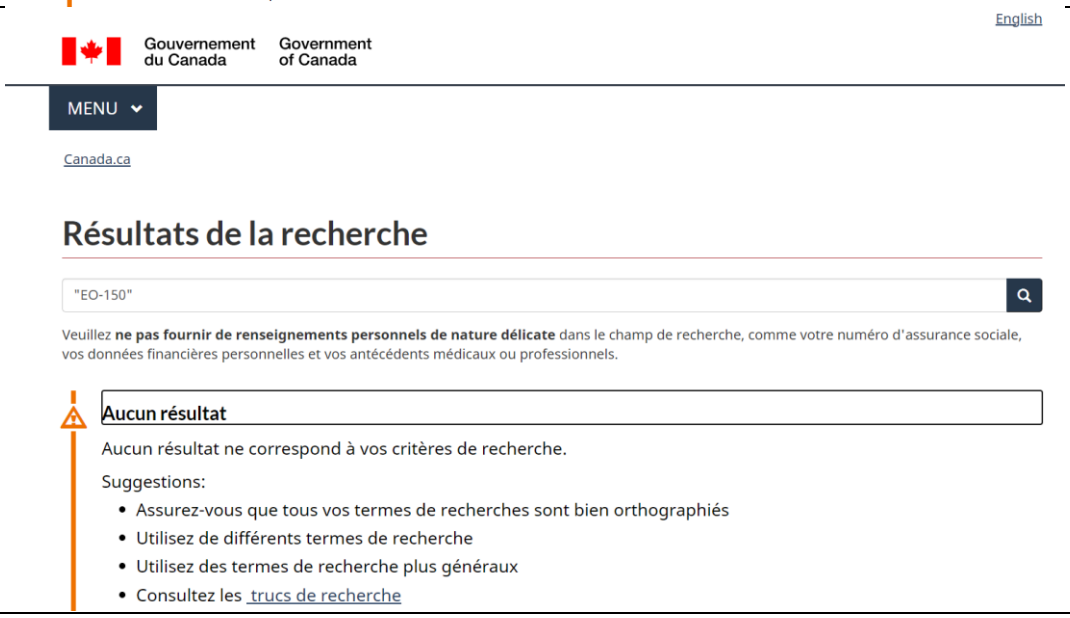
13.6 APPENDIX 6: VIGILANCE DATA FROM INTERNATIONAL DATABASE FOR EOVE, EO-150 AND HOME MECHANICAL VENTILATORS

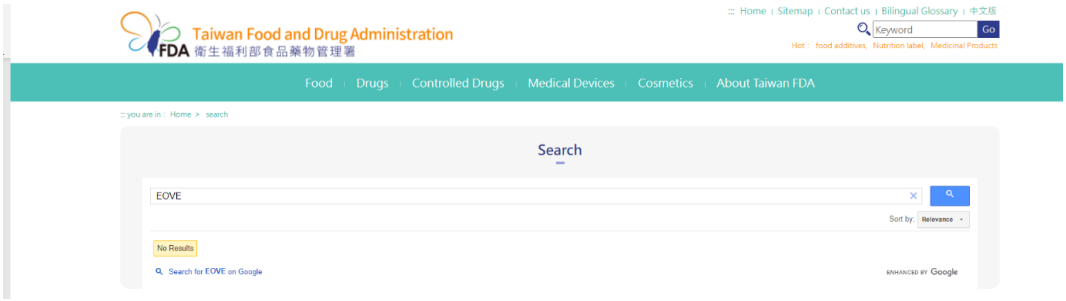
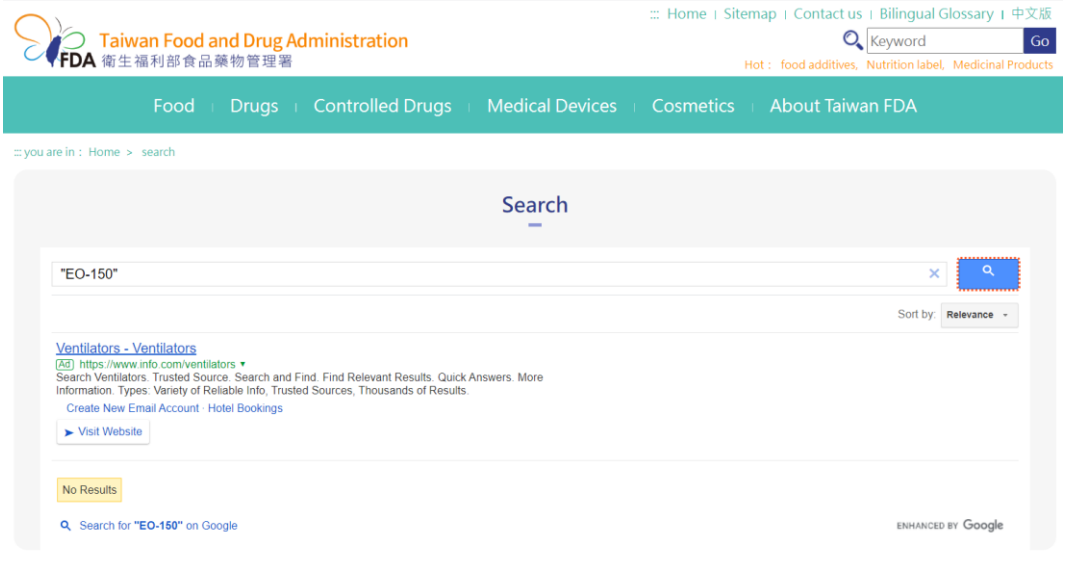
ANSM (France)	
EOVE: 4 hits	
E0-150: 3 hits	
“ventilateur à domicile”: 31 hits	
TPLC (USA)	

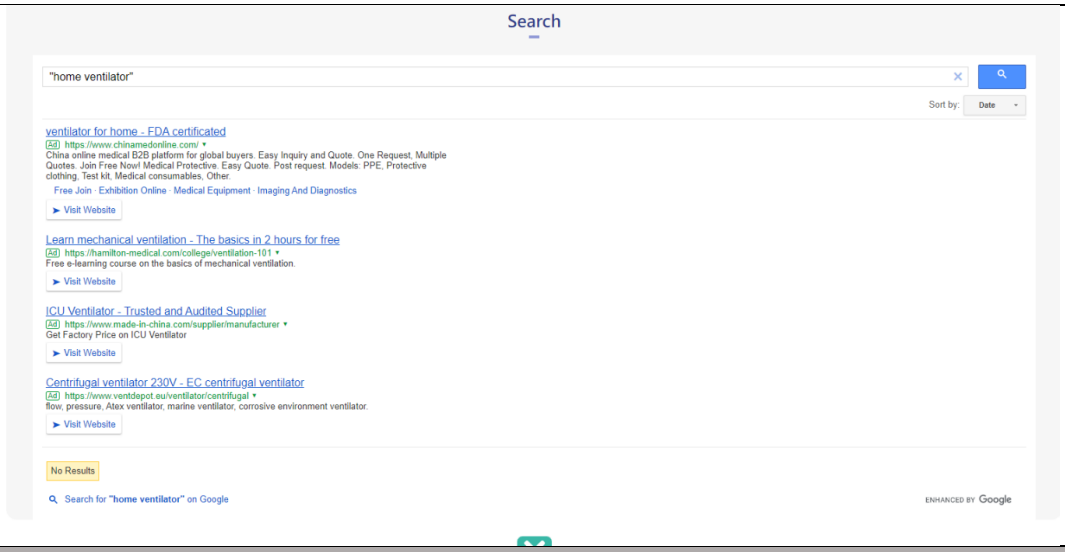
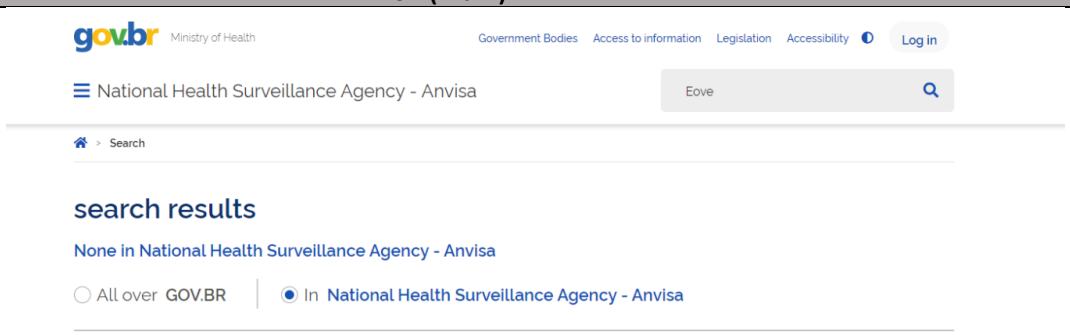
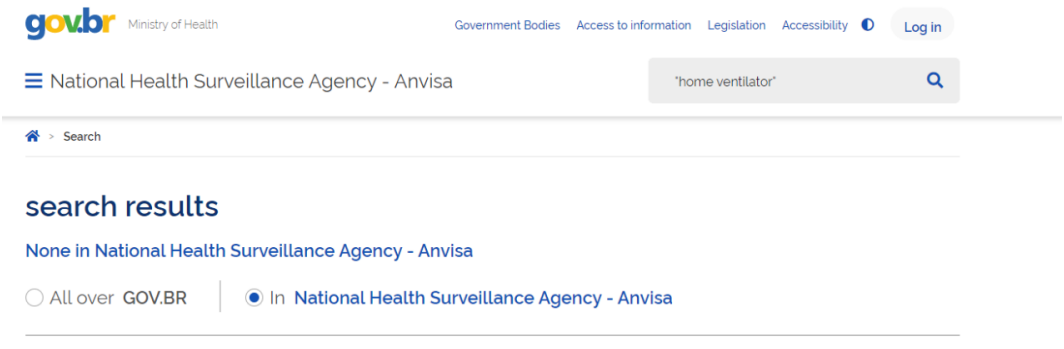
EOVE: 0 hits	
EO-150 : 0 hits	
"Home ventilator": 2 hits	
MAUDE (USA)	

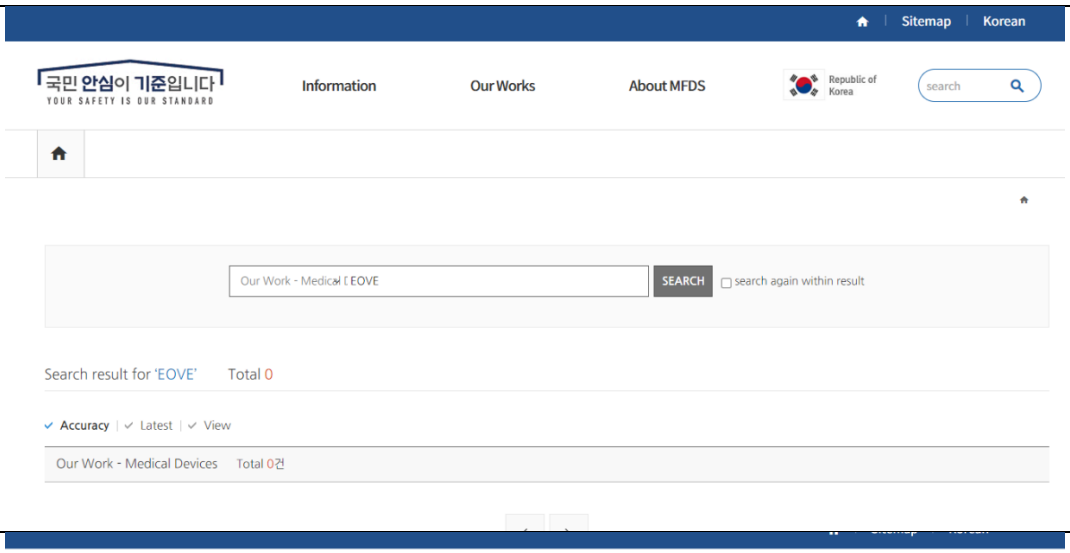
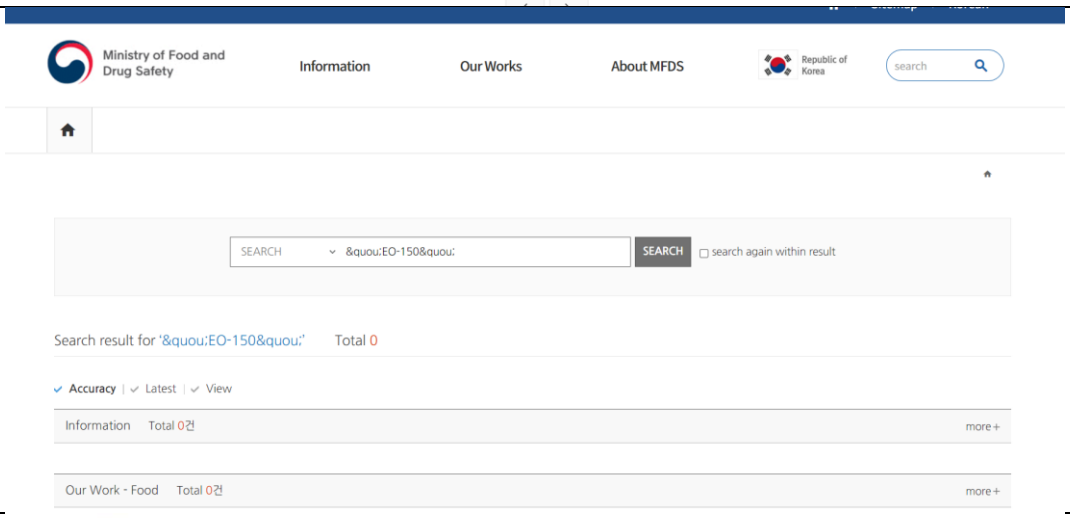
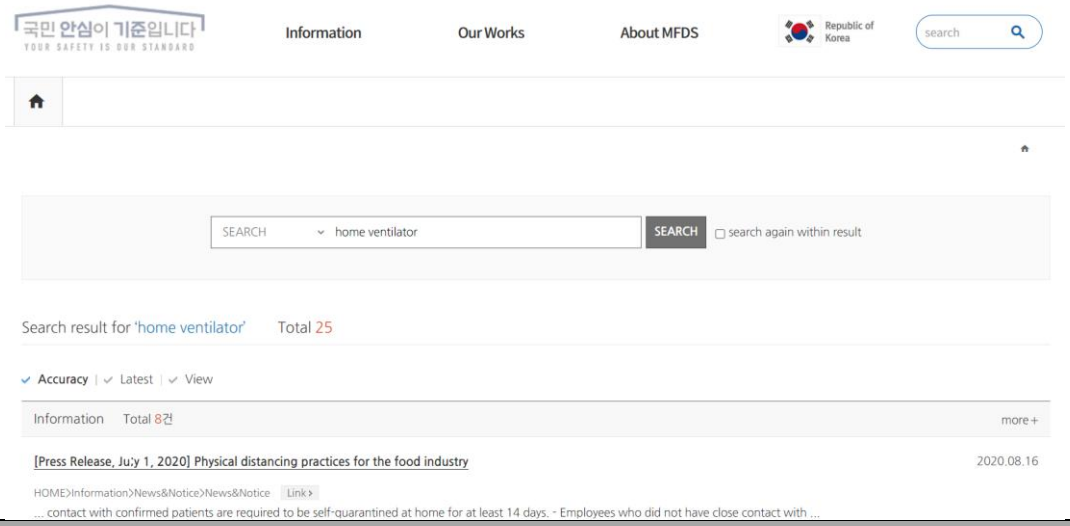
EOVE: 0 hits	
EO-150: 0 hits	
Category "Ventilator, Continuous, Minimal Ventilatory Support, Home Use": 0 hits	
Bfarm (Germany)	

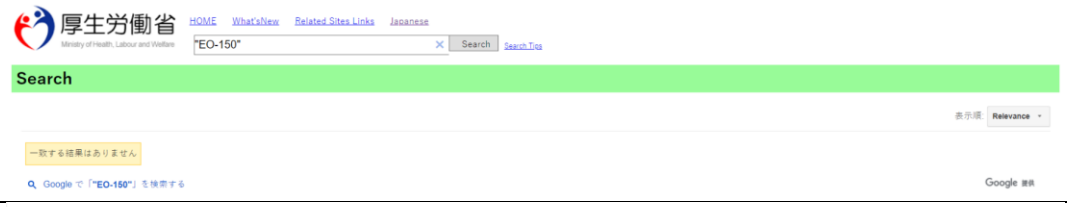
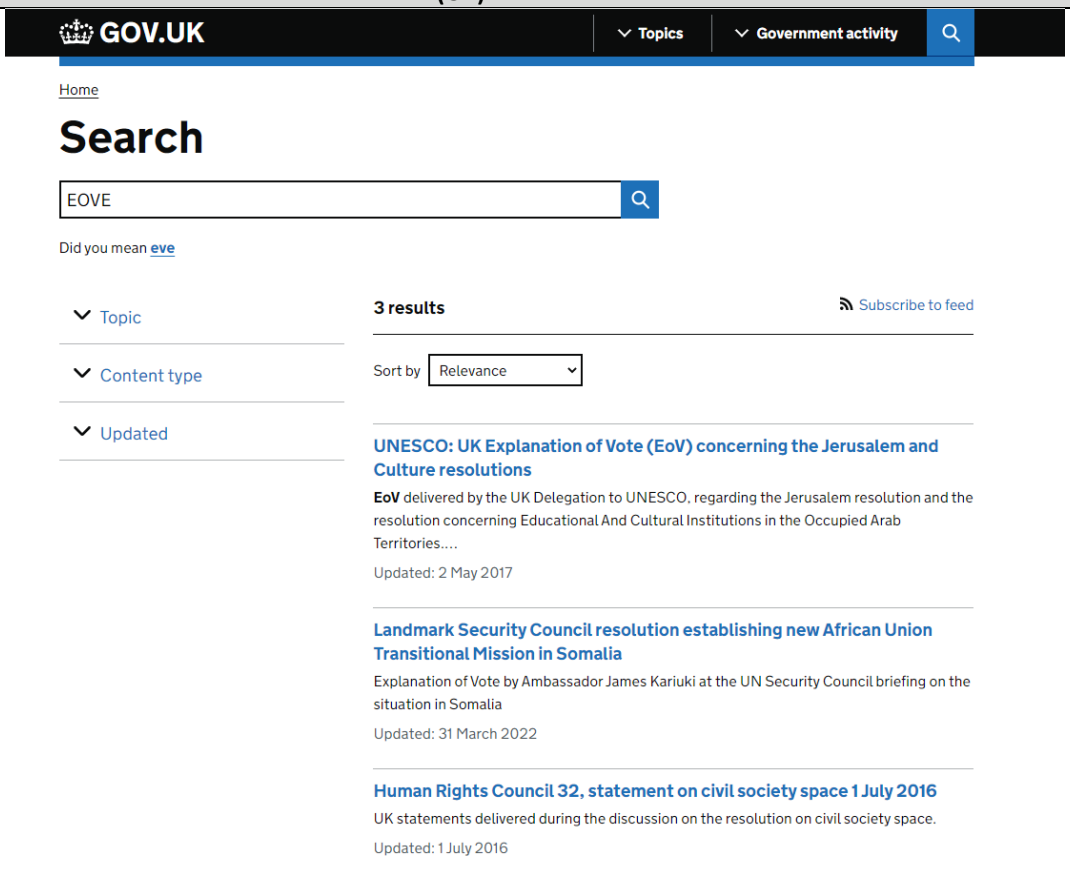
EOVE: 5 hits	
EO-150: 3 hits	

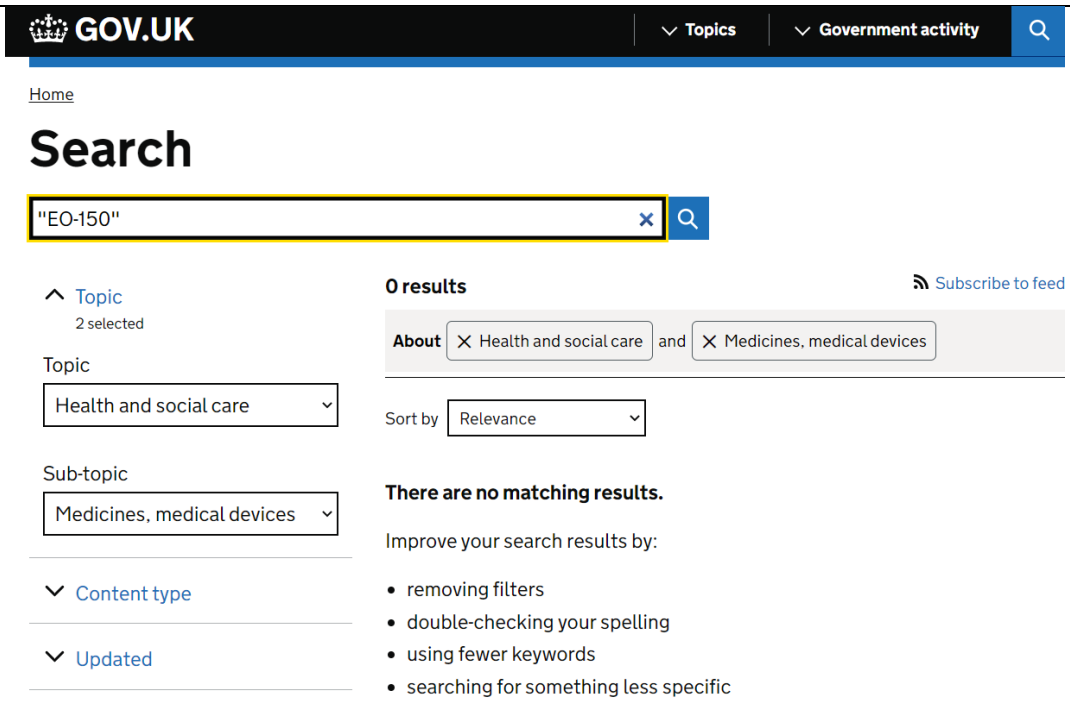
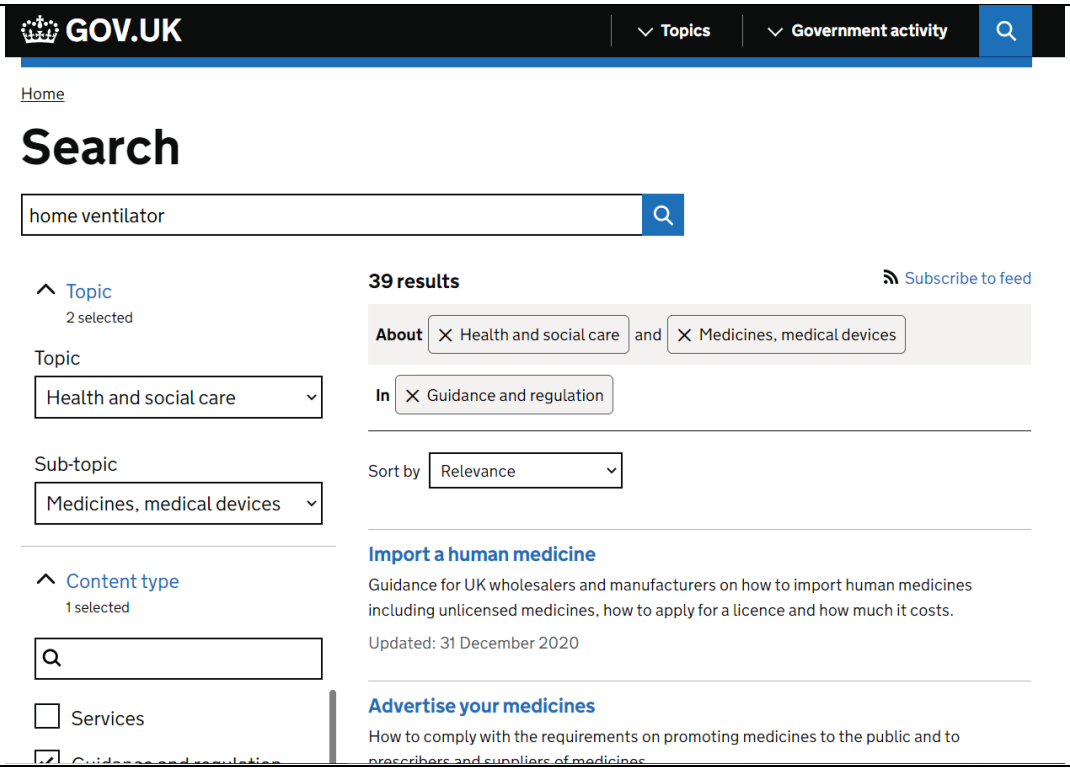
Home ventilator: 23 hits	
Santé Canada (Canada)	
EOVE: 0 hits	
EO-150: 0 hits	

"Home ventilator": 0 hits	
TFDA (Taiwan)	
EOVE: 0 hits	
EO-150: 0 hits	

"Home ventilator": 0 hits	
ANVISA (Brazil)	
EOVE: 0 hits	
EO-150: 0 hits	
"Home ventilator": 0 hits	
MFDS (South Korea)	

EOVE: 0 hits	
EO-150: 0 hits	
Home ventilator: 25 hits	
MHLW (Japan)	

EOVE: 0 hits	
EO-150: 0 hits	
"Home ventilator": 0 hits	
MHRA (UK)	
EOVE: 3 hits	

EO-150: 0 hits	
"Home ventilator": 39 hits	

13.7 APPENDIX 7: INFORMATION SUPPLIED WITH THE DEVICE

See electronic appendix "**100_23 revDE : user manual_EO-150**".

13.8 APPENDIX 8: BIOLOGICAL RISK ASSESSMENT

See electronic appendix "**100_69 Rev C - Biocompatibilty evaluation report EO150"**.

13.9 APPENDIX 9: STABILITY DATA

See electronic appendix "**100_616_B_lifetime evaluationEO150**".

13.10 APPENDIX 10: RISK MANAGEMENT DOSSIER

See electronic appendix "**100_15 - E - EO 150 Risk management plan", "100_17 AI Risk Analysis"** (word and excel files), **"100_67 - rev I - Risk management report"**.