EUROPEAN COMMISSION

Expert decision and opinion in the context of the Clinical Evaluation Consultation Procedure (CECP)

Expert panels on medical devices and in vitro diagnostic devices (Expamed)

Contents

Scope of this expert opinion

This scientific opinion reflects the views of independent experts (MDR Article 106) on the clinical evaluation assessment report (CEAR) of the notified body. The advice is provided in the context of the clinical evaluation consultation procedure (CECP), which is an additional element of conformity assessment by notified bodies for specific high-risk devices (MDR Article 54 and Annex IX, Section 5.1).

The notified body is obliged to give due consideration to views expressed in the scientific opinion of the expert panel and in particular in case experts find the level of clinical evidence not sufficient or have serious concerns about the benefit-risk determination, the consistency of the clinical evidence with the intended purpose including the medical indication(s) or with the post-market clinical follow-up (PMCF) plan.

Having considered the expert views, the notified body must, if necessary, advise the manufacturer on possible actions, such as specific restrictions of the intended purpose, limitations on the duration of the certificate validity, specific post-market follow-up (PMCF) studies, adaption of instructions for use or the summary of safety and clinical performance (SSCP) or may impose other restrictions in its conformity assessment report.

In accordance with MDR Annex IX, 5.1.g., the notified body shall provide a full justification where it has not followed the advice of the expert panel in its conformity assessment report.

1 ADMINISTRATIVE INFORMATION

Date of reception of the dossier	07/10/2024
Notified Body number	2696
Internal CECP dossier #	EMA/EX/0000232089
Medical device type	Mechanical Ventilator
Intended purpose	Artificially maintain the respiratory function in cases where the lung is failing.
Risk class / type	☐ class III implantable ☒ class IIb active device intended to administer or remove medicinal products(s)
Screening step: medical field / competence area	Respiratory

2 DECISION OF SCREENING EXPERTS: NOTIFICATION OF NB AND COMMISSION REGARDING THE INTENTION TO PROVIDE AN OPINION

2.1 Decision of the screening experts

Table covers all three criteria, intended to support their consistent and conscientious application

Date of decision	18/11/2024
Screening panel decision	
Is there intention to provide a scientific opinion?	☒ **Yes** ☐ **No** ☐ **Insufficient information to reach a conclusion**
In case the information was found insufficient to reach a conclusion: summary of reasons (see MDR Annex IX Section 5.1 point c)	
Not applicable	
Summary as to why there is intention to provide an opinion	
We consider that an opinion is needed. This is a new device in the market. There are inconsistencies in the documents presented by the NB. Those make us question the potential impact on health and the novelty of the device.	
Summary as to why there is *no* intention to provide an opinion	
Not applicable	
Any other comments	
Not applicable	

2.2 Assessment of the three screening criteria

Criterion 1: Novelty of device under assessment and possible clinical / health impact
1.1 Overall degree of novelty
☒ No novelty: Neither device nor clinical procedure is novel ☐ Low level of novelty ☐ Medium level of novelty ☐ High level of novelty
Short description of the novelty, including main dimension(s) of novelty
The experts did not detect any novel features in the design and/or function of the device in comparison with the reference ventilator as described in the NB's document.
1.2 Possible negative clinical / health impact resulting from novelty
Estimated* possible clinical and/or health impact related to the novel aspects of the device * This can entail uncertainty. Not only *known* clinical / health impacts but also *possible* ones (conceivable uncertainties, hazards, risks) should be taken into account but need to be supported by a scientific, clinical or technical reasoning.

☐ No clinical or health impact ☐ Minor clinical or health impact ☐ Moderate clinical or health impact ☒ Major clinical or health impact
Possible major clinical or health impact related to the novel aspects of the device
Numerous inconsistencies have been identified in the documents presented for the clinical evaluation consultation procedure, namely between the CER and the CEAR. These generate a high level of uncertainty regarding the possible impact of certain aspects of the device. Some examples: 1. Different names of the device; 2. Uncertainties on the device models being considered for the assessment; 3. The specific pictures and diagrams of the device; 4. The target population (from neonates to adults) and how this relates to the minimal tidal volume of the device (10ml or 50 ml); 5. The medical area of utilization (ICU, emergency, or homecare); 6. Inconsistencies in the indications and contraindications.

Criterion 2: Scientifically valid health concerns leading to significantly adverse changes in the benefit-risk profile of a specific group / category of devices and relating to **a) Component(s)** **b) Source material(s)** **c) Impact on health in case of failure of the device**	
2.1 Information received from Secretariat:	☐ Yes ☒ No
2.2 Other information available to experts:	☐ Yes ☒ No

Criterion 3: Significant increase of serious incidents of a specific group / category of devices relevant for the device under assessment ***(if information is available, it will always be provided by the expert panel secretariat)***	
3.1 Information received from secretariat?	☐ Yes ☒ No

2.3 Indication of appropriate thematic panel in case opinion is required

Indication of appropriate thematic panel and competence area		
	Expert panels	Medical and scientific/technical competence areas (these may correspond to sub-groups)
☐	**Orthopaedics, traumatology, rehabilitation, rheumatology**	☐ 1. Joint replacements (hip, knee, shoulder) ☐ 2. Spinal devices ☐ 3. Non-articulating devices, rehabilitation
☐	**Circulatory system**	☐ 1. Prosthetic heart valves and devices for heart valve repair ☐ 2. Cardiovascular stents (metallic and bio-resorbable) and vascular prostheses ☐ 3. Active implantable cardiac devices and electrophysiological devices ☐ 4. Structural interventions and new devices (e.g. LAA/PFO occluders, heart failure devices) ☐ 5. Cardiac surgery including extracorporeal membrane oxygenation, cardiopulmonary bypass devices, artificial hearts and left ventricular assist devices
☐	**Neurology**	☐ 1. Central and peripheral nervous system devices ☐ 2. Implants for hearing and vision (sensory recovery) ☐ 3. Neurosurgical devices
☒	**Respiratory, anaesthesiology, intensive care**	☒ Respiratory and anaesthetic devices
☐	**Endocrinology and diabetes**	☐ Endocrinology and diabetes devices
☐	**General and plastic surgery Dentistry**	☐ 1. Surgical implants and general surgery ☐ 2. Plastic surgery and wound care ☐ 3. Maxillofacial surgery & Devices for dentistry e.g. oral surgery, implantology, dental materials etc.
☐	**Obstetrics and gynaecology including reproductive medicine**	☐ Devices for obstetrics and gynaecology
☐	**Gastroenterology and hepatology**	☐ Devices for gastroenterology and hepatology
☐	**Nephrology and urology**	☐ Devices for nephrology and urology
☐	**Ophthalmology**	☐ Devices for ophthalmology

3 SCIENTIFIC OPINION OF THE THEMATIC EXPERT PANEL/SUB-GROUP

3.1 Information on panel and sub-group

Date of opinion	10/01/2025
Expert panel name	Respiratory system, anaesthesiology, intensive care
Sub-group of expert panel (where relevant)	Respiratory and anaesthetic devices

3.2 Detailed aspects of the opinion as required by MDR Annex IX Section 5.1

Opinion of the expert panel on the specific aspects of the clinical evaluation assessment report of the notified body (CEAR)[1]
1. Overall opinion on the NB's assessment of the manufacturer's clinical evaluation report
This expert panel found the following serious issues with both the documents presented by the NB for the clinical assessment and the documents presented by the manufacturer to the NB: • Inconsistencies were identified in those documents, namely between the Clinical Evaluation Plan (CEP), Clinical Evaluation Report (CER) from the manufacturer and the Clinical Evaluation Assessment Report (CEAR), affecting, among other things, properties and parameters critical for assessing clinical adequacy and safety. • The clinical evaluation is supported by a literature review that is limited both in scope and applicability to the specific device under consideration. Additionally, equivalence is claimed to an already marketed device. However, the clinical equivalence cannot be properly reviewed because of the inconsistencies mentioned (it is not clear to which device is the equivalence claimed), and incomplete documentation provided. Therefore, the panel considered there was insufficient information to allow a thorough assessment of the clinical impact of the device. • There were very few details provided in the Post-Marketing Clinical Follow-Up plan (PMCF plan). Given the uncertainties highlighted concerning the data provided for the pre-market clinical evaluation, the lack of details on the PMCF plan becomes even more significant to be able to evaluate the need for additional data in the post-marketing phase. The experts are particularly concerned about several issues related to the clinical evaluation, namely: 1) Insufficiency of the evidence about the safety of the device; 2) Absence of evidence that a meaningful clinical evaluation was performed and the lack of evidence supporting the adequacy of the device for the intended purpose and the chosen target population; 3) Serious mistakes on the pathophysiology of mechanical ventilation and its benefits but also on the risks for the patients; 4) Absence of a comprehensive PMCF plan; 5) The failure of the NB to detect and adequately address the issues explained in the previous points.

[1] According to Annex IX Section 5.1 of Regulation (EU) 2017/745 - Assessment procedure for certain class III and class IIb devices.

Moreover, the documents contained numerous errors and inconsistencies and overall were difficult to understand.

Given the fundamental issues with the quality and consistency of the documentation presented, it's questionable from the experts' perspective if incremental improvements as part of the current conformity assessment procedure can realistically lead to an adequate level of confidence in the assessment of the device's performance and safety in relation to the associated clinical risks, in particular given the fact that the device – with regard to its intended purpose as far as can be determined from the insufficient documentation provided - is in no way novel and thus cannot contribute to improvements in patient care beyond what is already achievable with available devices that could justify any level of additional risk. Therefore, the expert panel has concerns that the NB assessment of the CER has been adequately performed and that it has demonstrated the benefit risk profile of the device.

2. Opinion on the NB's assessment of the adequacy of the manufacturer's benefit-risk determination

This expert panel considers that the information provided regarding the benefit-risk determination is incomplete, insufficient and/or incorrect. The manufacturer's benefit-risk determination is mostly based on general assertions on the risks related to mechanical ventilation.

3. Opinion on the NB's assessment of the consistency of the manufacturer's clinical evidence with the intended purpose, including medical indication(s)

The NB's assessment as presented in the CEAR consist of a general and well-known list of indications and contraindications on the uses of mechanical ventilation and not specific to this device.

Additionally, there are relevant mistakes and inconstancies within the CEAR or linked to the CER and the CEP that result in a difficulty to understanding the key aspects of the device, for example:

- The name of the equipment: in the CEAR it is referred as AirVENT60 and in the CER it is referred to as Vent 2. No explanation for the discrepancy is presented.
- The target population: based on the CEAR, the device is intended for adults and children with tidal volumes > 50 ml (>5 kg), whereas in the CER, a lower limit of 10 ml (>1 kg) is stated. In real life tidal volumes > 50ml are not suitable for neonates and most infants. No explanation for the discrepancy is presented.
- The intended use: based on the CEAR, the device can be used via tracheostomy or using a mask. However, there is no mention of an endotracheal tube as part of the equipment.
- The clinical benefits of ventilators according to the CEAR include "reducing intracranial pressure". While this may occur in very specific clinical circumstances, usually what happens with mechanical ventilation is the increase of intracranial pressure.
- In the section "Warnings for oxygen usage", it is mentioned that "oxygen supply must be terminated before ventilation is interrupted. It is also recommended that at the end of ventilation the device be operated without oxygen supply for several ventilation cycles." (CER, p23). This is confusing, as it is not possible to safely interrupt the oxygen supply as part of standard application scenarios of a mechanical ventilator connected to a patient.
- In the PMCF plan, the patients to be included in the study "must be receiving mechanical ventilation therapy in the outpatient settings (e.g. clinics, sleep centres)" and the patients to be excluded are the ones that are "intubated or have a tracheostomy". This contradicts other documents that mention that the device is intended for hospital use only.

- The quality and content of the figures presented is poor, creating difficulties in reading and interpretation of the information provided.

4. Opinion on the NB's assessment of the consistency of the manufacturer's clinical evidence with the PMCF plan

The PMCF plan is inconsistent and error-ridden, and it is unclear on which clinical settings and for which patient groups the device is intended to be used.

The manufacturer planned a study to evaluate adverse events in outpatient settings only on non-intubated and without tracheostomy patients. By doing so, the manufacturer is failing to investigate other important stated clinical indications for his type of device in its application on intubated and mechanically ventilated patients.

In the PMCF plan, the manufacturer proposed several goals, but it is unclear if the study aims to detect any particular adverse events. It can be seriously hazardous to only detect adverse events after a certain period of use of the device, and not planning for a possible early intervention on the device if a serious malfunction occurs.

The PMCF plan also fails to identify possible systematic misuse and off-label use of the device to verify its correct use.

In summary, the PMCF plan has been poorly written, and even assuming the lowest-risk application scenarios, is considered inadequate to achieve its objectives.

3.3 Summary of expert panel opinion

The CEAR submitted appears to contain many errors and inconsistencies in the document itself and also compared to the information provided in the CER and CEP documents.

The description of the device, its intended purpose, target population and indications/contraindications are either incomplete or presented in an inconsistent way, and the CEAR contains very limited clinical information related to the device itself, mostly listing generally known facts about this type of equipment. The intended purpose presented in the PMCF plan section of the CEAR is inconsistent with what is presented in the PMCF plan of the manufacturer.

Overall, this expert panel considers this CEAR as being of poor quality, failing to provide the clinical data needed to thoroughly assess the safety and performance of the device.

3.4 Recommendations

Based on all the issues raised before, this expert panel has the following recommendations:

- A thorough review of all the documentation presented to this clinical evaluation consultation procedure is required, with careful correction of the mistakes and inconsistencies.
- Update of the clinical data presented for the assessment: improve the shortcomings of the literature review and solve the inconsistencies regarding the clinical equivalence claimed by the manufacturer.
- Further develop the PMCF plan by presenting more details on the proposed study(ies) and ensure that those are clearly targeting the gaps of knowledge identified in the pre-market phase.
- Harmonise the wording of the intended purpose of the device in all the documents and ensure that all patients that would benefit from the use of the device are captured in the follow-up study(ies).

3.5 Stakeholder information, where available

Relevant information provided by stakeholders, if applicable[2]
Has the Secretariat provided information from stakeholders?
☐ Yes ☒ No
Summary of the information that was taken into account and how it was taken into account.
Not applicable

3.6 Divergent positions in case no consensus was reached

Please indicate how many of the experts of the panel or sub-group had divergent views
None
Summary of divergent positions
Not applicable

[2] According to Article 106.4 of Regulation (EU) 2017/745, expert panels shall take into account relevant information provided by stakeholders including patients' organisations and healthcare professionals when preparing their scientific opinions.